

Cost-effectiveness analysis of interventions to prevent cardiovascular disease in Vietnam

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Background	Vietnam is in the process of an epidemiological transition, with cardiovascular disease (CVD) now ranked as the leading cause of death. The burden of CVD will continue to rise unless effective interventions for addressing its underlying risk factors are put in place.
Objectives	To assess the costs, health effects and cost-effectiveness of a set of personal and non-personal prevention strategies to reduce CVD in Vietnam, including mass media campaigns for reducing consumption of salt and tobacco, drugs for lowering blood pressure or cholesterol, and combined pharmacotherapy for people at varying levels of absolute risk of a cardiovascular event.
Methods	WHO-CHOICE methods and analytical models were employed, using local data to estimate the costs, effects and cost-effectiveness of 12 population and individual interventions implemented singly or in combination. Costs were measured in Vietnamese Dong for the year 2007 (discounted at a rate of 3% per year), while health effects were expressed in age-weighted and discounted disability-adjusted life years (DALYs) averted.
Results	A health education programme to reduce salt intake (VND 1 945 002 or US\$118 per DALY averted) and individual treatment of systolic blood pressure above 160 mmHg (VND 1 281 596 or US\$78 per DALY averted) were found to be the most cost-effective measures for population- and individual-based approaches, respectively. Where budget is very limited, a mass media education programme on salt intake and a combination mass media programme addressing salt intake, cholesterol and tobacco should be selected first. If more resources become available, greatest population health gains can be achieved via individual treatment of systolic blood pressure and the absolute risk approach to CVD prevention.
Conclusions	Contextualization of WHO-CHOICE using local data provides health decision-makers with more sound economic evidence for policy debates on prioritizing health interventions to reduce cardiovascular diseases in Vietnam. When used, cost-effectiveness analysis could increase efficiency in allocating scarce resources.
Keywords	Cost-effectiveness, cardiovascular disease, systolic blood pressure, cholesterol, salt intake, Vietnam

KEY MESSAGES

- The most efficient preventive interventions to reduce risk factors for cardiovascular disease in Vietnam are highly cost-effective (each healthy year of life gained costs less than average annual income per capita).
- With no budget constraint, the single most cost-effective preventive strategy is individual treatment of systolic blood pressure over 160 mmHg, followed by combination drug therapy for individuals with an elevated risk of experiencing a CVD event over the next 10 years. If resources are highly restricted, population-based mass media strategies aimed at reducing levels of cholesterol and dietary salt intake become the most probable interventions to implement.
- Using local and context-specific information to apply generalized cost-effectiveness methods at the national level offers a promising approach to improved evidence-based health policy-making in developing countries.

Introduction

Background

Cardiovascular disease (CVD) is the leading cause of morbidity and mortality worldwide, with 80% of total deaths occurring in developing countries (WHO 2002). The most common causes of CVD morbidity and mortality are ischemic heart disease (IHD), stroke and congestive heart failure (CHF). Risk factors include, amongst other things, tobacco use, high blood pressure, high cholesterol level, high body mass index and alcohol consumption. Among these risk factors, smoking, high systolic blood pressure and cholesterol concentration account for more than 70% of the burden of CVD (Ezzati 2004).

Vietnam has been undergoing an epidemiological transition, in which the overall morbidity and mortality pattern has shifted from communicable diseases to non-communicable diseases. Increased non-communicable diseases leave the country with a double financial burden, resulting from an established high burden of infectious diseases and at the same time the escalating morbidity and mortality of non-communicable diseases such as diabetes, cancer and especially CVD. In addition, Vietnam has a very high injury burden, mainly as a result of road traffic injuries, prompting the concept of the triple burden of disease. A recent national burden of disease study conducted in 2008 (T Vos, personal communication, 2009) found that cardiovascular diseases, mainly strokes and IHD, account for one-third of total deaths, and are ranked first among the top 10 leading causes of mortality. Moreover, these diseases were found to make up the largest share (approximately 20%) of the total burden of disability-adjusted life years (DALYs) lost.

Evidence has shown that key risk factors for CVD in Vietnam are either on the rise or already at alarming levels. First, the Vietnam National Health Survey (VNHS) 2001/02 estimated that the prevalence of hypertension was 16.9% among people aged 25–65 years (MOH 2003), a 51% increase compared with 1992. By 65 years of age around half of all men and women suffer from hypertension. Secondly, analyses using Vietnam Living Standards Survey 1992/93 and VNHS 2002/03 showed an increased trend for the prevalence of overweight and obesity (Tuan *et al.* 2008). In addition to this, a recently conducted study (Cuong *et al.* 2007) found that the prevalence of overweight and obesity in adults is 6.4% in Ho Chi Minh City, signalling an emerging public health problem in urban areas. Thirdly, cooking culture and habitual eating preferences for using salt predominantly in preserving meat and fish, and

in seasoning and sauces used during cooking and at the table, make the salt intake level of the Vietnamese higher than the level recommended by the World Health Organization (WHO) of 5 grams per day (WHO 2003). Fourthly, awareness around CVD risk factors among the Vietnamese is relatively low (approximately 50%), but considerably lower than this in rural areas (Khai *et al.* 2008). Finally, a smoking prevalence of 56% among Vietnamese males aged over 16 years places them among the heaviest smokers in the world (MOH 2003).

Evidently, the burden of cardiovascular diseases will continue to increase in Vietnam unless effective strategies for addressing risk factors are in place. While further increases in both internal and external financing for CVD control and prevention programmes are needed, it is extremely important for the current resources to be used efficiently. A recognized tool for guiding resource allocation is cost-effectiveness analysis. A decade ago, the WHO introduced WHO-CHOICE (CHOosing Interventions that are Cost Effective) with the intention of assisting resource allocation in the health sector, both at the global and national levels (Murray *et al.* 2000). Key aspects of the WHO-CHOICE approach to cost-effectiveness analysis are described in detail elsewhere (Adam *et al.* 2003; Edejer *et al.* 2003; Hutubessy *et al.* 2003; Lauer *et al.* 2003). Regional information on costs and population health effectiveness of these diseases has been made available on the WHO website (<http://www.who.int/choice/en/>), as are further details on the WHO-CHOICE approach and methodology.

Study objective

By applying WHO-CHOICE models and using locally available data, the overall objective of this study is to inform policy makers about the costs, effects and cost-effectiveness of preventive interventions, and how they can be combined efficiently to prevent and reduce CVD risk factors in Vietnam. Such application of WHO-CHOICE models for cost-effectiveness analysis of interventions to reduce CVD in Vietnam is promising and realistic for a couple of reasons. First, the ingredient approach developed by WHO-CHOICE allows country analysts to adapt regional-level information down to the national level. Second, several surveys such as risk factors of non-communicable diseases and burden of disease, which have been recently carried out in Vietnam, provide valuable national demographic and epidemiological parameters for modelling population effectiveness. With respect to health policy, the contextualization of WHO-CHOICE will enable the Ministry of

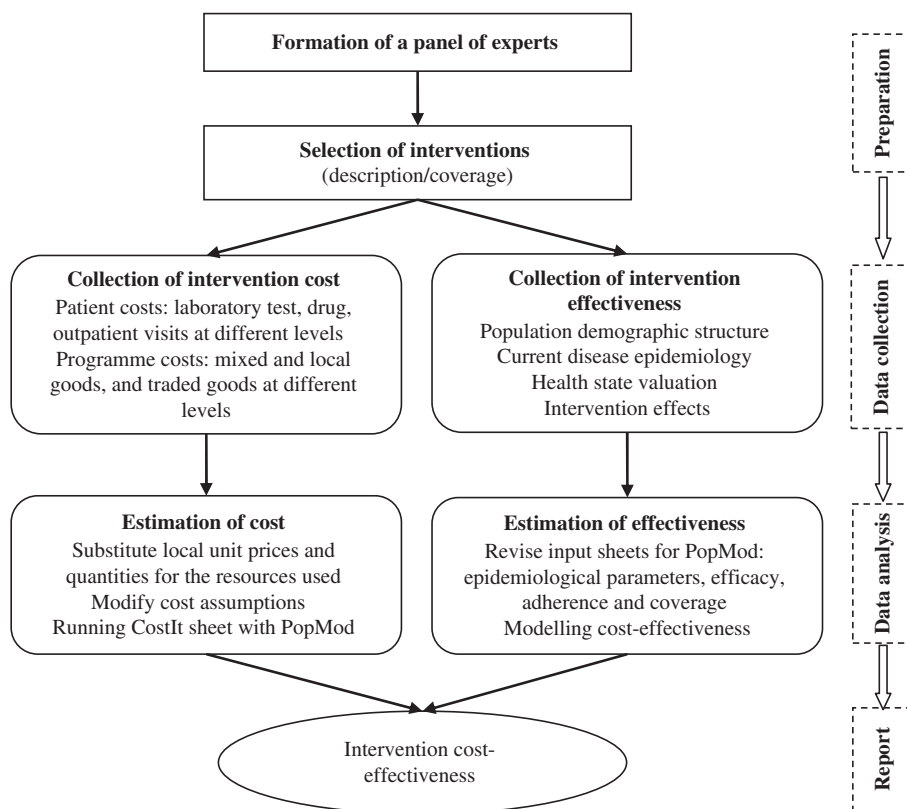


Figure 1 Methodological framework of WHO-CHOICE analysis

Health to know whether or not the resources currently devoted to cardiovascular prevention programmes achieve as much health effectiveness as they could; and how best to use additional resources if they become available.

Methods and data

Overview of WHO-CHOICE contextualization process

Figure 1 provides a methodological framework within which WHO-CHOICE estimates and models can be translated to the context of Vietnam. There are four key phases for the contextualization. In the first phase, we formed a panel of experts including Vietnamese experts in health economics, epidemiology, public health, and health communication and education. Based on their expertise and knowledge of Vietnam's health situation, the experts advised us on the selection of interventions and, more importantly, helped to re-adjust the prices and quantities provided by WHO-CHOICE, as well as the current coverage of interventions. The second and third phases involved data collection and subsequent modelling of intervention effectiveness and costs at the population level, as described in detail below. The final phase concerns the assimilation of costs and effects data into estimates of intervention cost-effectiveness, including assessment of the extent to which baseline findings are sensitive to plausible changes to key input parameters.

Description of interventions and their effects

Preventive interventions for CVD fall into two categories: population-wide and personal interventions, targeting the general population and individuals who are at high risk, respectively. The former is based on the concept that the majority of cases of CVD occur among persons with medium and low levels of risk (Rose *et al.* 2008). Achieving a small change in risk factors in the population at large may bring greater benefits than a large change in a sub-population of high-risk cases (Kottke *et al.* 1988).

Individual interventions were selected based on published studies (Murray *et al.* 2003; Gaziano *et al.* 2006), and experts' opinion (see Table 1). Population-wide interventions are comprised of three separate health education programmes aimed at reducing salt intake, cholesterol levels and tobacco consumption through mass media, together with a combined mass media strategy (for which we assumed an additive effect due to the fact that each of the individual campaigns target a specific and distinct risk factor). Health education messages are modelled to be broadcasted on television and radio channels at both central and provincial levels, as well as communicated in print via newspapers, wall posters and fliers/leaflets. In the particular case of the salt reduction strategy, we also include a voluntary agreement among manufacturers of processed foods to reduce salt content levels.

Individual interventions are divided into two sub-groups: individual treatment based on elevated levels of systolic blood pressure and cholesterol, and individual treatment based on the

Table 1 Interventions and their effects

Code	Description of intervention	Outcome affected	Estimate of effect [uncertainty range used]	Sources
P1	Health education through the mass media to reduce salt intake and a voluntary reduction in salt content of processed foods	Total dietary salt intake	-20% [10-30%]	(Law <i>et al.</i> 1991; Tian <i>et al.</i> 1995; He <i>et al.</i> 2002; Murray <i>et al.</i> 2003; Forrester <i>et al.</i> 2004; Asaria <i>et al.</i> 2007)
P2	Health education through the mass media to reduce smoking	Prevalence of smoking	-1.5% [0.8-2.3%]	(Friend and Levy 2002; Levy <i>et al.</i> 2006)
P3	Health education through the mass media to reduce cholesterol concentrations	Total blood cholesterol	-2% [1-3%]	(Fortmann <i>et al.</i> 1981; Puska <i>et al.</i> 1983; Farquhar <i>et al.</i> 1990)
P4	Combined mass media strategy (P1 - P3)	As above	As above	
I1-I2	Education and individual treatment (β-blocker and diuretic) for high systolic blood pressure (≥140 mmHg and ≥160 mmHg)	Difference between actual systolic blood pressure and 115 mmHg	-28% [23-33%]	(MacMahon <i>et al.</i> 1990; Collins <i>et al.</i> 1990; MacMahon and Rodgers 1993; Collins and MacMahon 1994; Prospective Studies Collaboration 1995; Gueyffier <i>et al.</i> 1997; Eastern Stroke & Coronary Heart Disease Collaborative Research Group 1998; Neal <i>et al.</i> 2000; Murray <i>et al.</i> 2003)
I3-I4	Individual treatment (statins) for cholesterol concentration (>5.7 mmol/l and >6.2 mmol/l)	Total blood cholesterol	-20% [17-23%]	(Tikkanen <i>et al.</i> 1988; Bradford <i>et al.</i> 1991a; Bradford <i>et al.</i> 1991b; Stein <i>et al.</i> 1993)
I5-I8	Combination treatment with β-blocker, diuretic, statins and aspirin for individuals with absolute risk of cardiovascular event (5%, 15%, 25%, 35% risk)	Absolute risk of CVD	Combined effect of I2 + I3 + additional 18% [15-21%] reduction of absolute risk for antiplatelet therapy	(Antithrombotic 2002; Murray <i>et al.</i> 2003)

absolute risk of a cardiovascular event in the next 10 years. Individual treatment to reduce systolic blood pressure comprises a regime of 50 mg per day atenolol and 25 mg per day hydrochlorothiazide for those who have elevated levels of systolic blood pressure of ≥140 mmHg (I1) or >160 mmHg (I2). Cholesterol-lowering drug treatment including 40 mg per day simvastatin is offered for those who have elevated cholesterol for two thresholds of cholesterol concentration >5.7 (I3) and mmol/l >6.2 mmol/l (I4). Individual treatment based on the absolute risk of a cardiovascular event over 10 years was assessed at four separate levels (5%, 15%, 25% and 35%; I5-I8), which has typically consisted of a regime of aspirin, diuretic, β-blocker and statin (Williams 2006). However, the choice of first-line drugs remains the subject of debate, especially concerning antihypertensive drugs in those without existing CVD (Antithrombotic Trialists Collaboration 2002; Dahlof *et al.* 2005). The regime proposed for this analysis is based on the traditionally proposed regime of 100 mg per day aspirin, 25 mg per day hydrochlorothiazide, 50 mg per day atenolol and 40 mg per day simvastatin.

Effectiveness estimates, expressed in terms of percentage improvements to the outcome of interest (such as total cholesterol level or daily salt intake), were taken from systematic reviews of randomized trials, meta-analyses and published articles on cost-effectiveness analysis (Table 1). For all individual interventions, and as advised by the panel of experts, a compliance rate of 50% was applied.

Modelling the impact of CVD preventive measures on disease outcomes

Estimation of the impact of CVD preventive strategies on final disease outcomes is quite complex, since there is a causal chain of effects that needs to be accounted for (or put another way, available evidence of intervention effect does not directly relate to a disease endpoint such as the incidence of stroke, but rather to underlying risk factors that are known to increase the probability of having a stroke). Accordingly, analysis comprised a number of steps. First, modelling was employed to estimate expected rates of disease incidence (specifically, IHD and stroke) that would occur in the population with and without the implementation of the prevention measures. This step was undertaken by means of a simulation model—based on the Asia Pacific Cohort Studies Collaboration—that applies the aforementioned effect sizes to the observed risk factor profile of different age and sex groups in the Vietnamese population (Table 2). Stata 10 (Stata Corporation, Texas, USA) was employed using a syntax specifically developed by WHO-CHOICE for this process.

Second, PopMod (version 4.5), one of the WHO-CHOICE tools, was used to estimate the lifetime health gains experienced by the Vietnamese population as a result of these intervention-induced changes in disease incidence. It has been described in detail by Lauer *et al.* (2003). PopMod tracks what would happen to each age and sex cohort in the Vietnamese population over a lifetime period (taken to be 100 years), first without any CVD prevention measures in place and then with the various interventions in place for the initial 10 years only (after which incidence rates go back to their 'non-intervention'

Table 2 Epidemiology of cardiovascular disease (CVD) and risk factors in Vietnam

Gender/age (years)	Disease incidence		Systolic blood pressure (mmHg)				Total blood cholesterol (mmol/L)				Smoking (prevalence)		Daily salt intake
	IHD (per 1000)	Stroke (per 1000)	Mean	S.D.	Relative risk for IHD	Relative risk for stroke	Mean	S.D.	Relative risk for IHD	Relative risk for stroke	Mean	Relative risk for CVD	NaCl per day
Male													
30–44	0.3	0.1	117.1	14.9	1.07	1.09	4.5	1.1	3.65	1.48	0.72	2.43	11.2
45–59	1.0	0.5	125.9	20.7	1.05	1.07	4.6	1.1	2.08	1.35	0.68	2.43	10.8
60–69	2.1	1.9	133.2	25.5	1.03	1.05	4.7	1.2	1.55	1.25	0.58	1.84	10.8
70–79	2.3	2.1	136.1	27.5	1.02	1.03	4.8	1.1	1.42	1.17	0.47	1.7	10.8
80+	4.4	3.5	136.1	27.5	1.01	1.02	4.8	1.1	1.42	1.09	0.3	1.38	10.8
Female													
30–44	0.5	0.3	110.6	14.6	1.07	1.09	4.3	1	3.65	1.48	0.01	2.43	10.1
45–59	4.5	3.0	122.4	20.3	1.05	1.07	4.8	1.1	2.08	1.35	0.03	2.43	9.7
60–69	20.0	12.3	132.3	25	1.03	1.05	5.1	1.3	1.55	1.25	0.05	1.84	9.7
70–79	40.9	32.6	136.2	26.9	1.02	1.03	5.1	1.2	1.42	1.17	0.04	1.7	9.7
80+	57.6	53.2	136.2	26.9	1.01	1.02	5.1	1.2	1.42	1.09	0.02	1.38	9.7

Note: IHD = ischemic heart disease.

Data sources: Disease incidence: Viet Nam burden of disease study (T Vos, personal communication, 2009); Blood pressure: Viet Nam Risk Factor Surveys (Khai *et al.* 2008); Smoking: Vietnam National Health Survey (MOH 2003); Blood cholesterol and all relative risk estimates: The Comparative Risk Assessment Project (Ezzati 2004); Salt intake: InterSalt study (Intersalt 1998).

levels). Thus, the difference in healthy years lived (which is equivalent to the number of disability-adjusted life years or DALYs incurred) by the population with versus without intervention provides our estimate of population-level intervention effect. DALYs in the base case analysis were age-weighted and discounted at an annual rate of 3%.

For the current epidemiology of IHD and stroke, including estimates of the average level of disability associated with these health conditions (on a 0–1 scale, where 0 denotes no disability), we used data from the national burden of disease study in Vietnam (T Vos, personal communication, 2009). Prevalence information of systolic blood pressure and smoking was collected from the 2001 and 2008 risk factor surveys (Khai *et al.* 2008) and Vietnam National Health Survey 2001/02 (MOH 2003), respectively, while the relative risks for IHD and stroke per unit increase in each risk factor were based on the estimates of WHO's Comparative Risk Assessment Project for the Western Pacific Region B (Ezzati 2004). Baseline salt intake profile was drawn from the InterSalt study (Intersalt 1988) (see Table 2). Data on demography and mortality rates by gender and age group were taken from the United Nations Population Division's Bureau for the year 2007.

Intervention costs

Costs are comprised of programme and patient-related costs. Programme costs are those incurred at the national, provincial and district administrative levels above the health facility level itself (such as training, programme administration and mass media), while patient costs are costs at the point of delivery consisting of diagnostic and laboratory tests, consultation, drugs, and hospital and health centre visits. Total costs were obtained by multiplying quantities by prices. To estimate the

costs, the entire set of ingredients and their quantities developed by WHO-CHOICE for interventions to reduce CVD were re-evaluated by the local panel of experts, making them more appropriate to the context of Vietnam.

In terms of resource quantities, and in addition to the drug regimens described above, all individual preventive strategies require laboratory tests (measuring blood pressure, cholesterol concentration and blood sugar), four health care provider visits per year, and 1.5 outpatient visits per year for health education. Population-based strategies, by contrast, use up programme management staffing inputs and mass media resources (for example, six weekly TV and radio emissions at the national level and two weekly emissions in each province were modelled for the salt and tobacco campaigns).

Prices/unit costs of the ingredients were collected from a variety of sources. Concretely, prices of drugs were derived from the International Drug Price database published by Management Sciences for Health (MSH) in 2007 (Table 3) (MSH 2007). These prices were added with a mark-up of 30% for transportation and distribution, as estimated by Hutton and Baltussen (2005). Personnel payment norms were based on salary scales used by the European Union and United Nations agencies in Vietnam (UN-EU 2007) and the Government regulation (Government of Vietnam 2004). Prices of media and other IEC material were taken directly from Vietnam Television, Voice of Vietnam, local television and radio stations, and Thanh Nien publishing. Unit costs for inpatient and outpatient care were based on a Vietnamese costing study conducted at central, provincial and district levels (Flessa and Dung 2004).

A costing template (CostIt) developed by WHO-CHOICE was employed to aggregate cost components over the intervention

Table 3 Unit costs for health intervention resource inputs

Domain	Measure	Vietnamese Dong	US\$
Secondary care	District hospital	11 330	0.69
	Provincial hospital	14 902	0.91
Primary care	10 minutes per visit	19 186	1.17
	20 minutes per visit	22 880	1.39
Drugs			
Aspirin	100 mg dose	36	0.002
Atenolol	50 mg dose	138	0.008
Hydrochlorothiazide	25 mg dose	49	0.003
Simvastatin	40 mg dose	657	0.04
Diagnostic tests			
Renal function		6904	0.42
Serum lipids		8918	0.543
Blood glucose		3596	0.219
Total cholesterol		4890	0.298
Hepatic function		13 233	0.806
Salaries (gross per year)			
Nurses		39 503 128	2406
Health worker		22 981 595	1400
Medical specialist		91 895 543	5596
Medical officer		63 744 761	3882
Programme director		91 895 543	5596
Programme manager		63 744 761	3882
Administration officer		39 503 128	2406
Secretary/receptionist		22 981 595	1400
Media (national level)			
Television time	1 minute	21 067 271	1282.95
Radio time	1 minute	2 532 665	154.23
Newspapers	1/4 page advertisement	17 585 554	1070.92
Wall posters	1 square metre	6589	0.40
Flyers/leaflets	A4 size	1387	0.08
Media (provincial level)			
Television time	1 minute	3 805 795	231.77
Radio time	1 minute	457 525	27.86
Newspapers	1/4 page advertisement	3 176 824	193.47
Wall posters	1 square metre	6589	0.40
Flyers/leaflets	A4 size	1387	0.08
Per diems (national level)		395 042	24

Sources: Drug prices: MSH (2007); inpatient and outpatient care: Flessa and Dung (2004); salaries: UN-EU (2007) and Government of Vietnam (2004); media and other IEC material prices: from Vietnam Television, Voice of Vietnam, local television and radio stations, and Thanh Nien publishing.

implementation horizon (10 years). All costs beyond the base year were discounted at a rate of 3% per year, consistent with other guidelines (Gold *et al.* 1996; Drummond 2005). Capital and start-up costs were likewise annualized over the assumed life-time of the intervention. Moreover, to adjust for capacity utilization, we assumed a norm of 80% for capacity utilization as recommended by WHO-CHOICE. Throughout this paper, all costs were estimated using societal perspective and Vietnamese Dong (VND) with an exchange rate of US\$1 = VND 16 421 for the base year 2007.

Calculating cost-effectiveness

When calculating cost-effectiveness ratios, we considered what would happen from today if all resources could be re-allocated. Put another way, the cost-effectiveness of each intervention was assessed in relation to the null or counterfactual scenario, in which none of the proposed interventions was implemented; this is the average cost-effectiveness ratio. In addition, we calculated incremental cost-effectiveness ratios for (non-dominated) interventions that fall on the efficiency frontier or cost-effectiveness

expansion path (see Figure 2 for a graphical demonstration of this concept).

Classification of cost-effective interventions was based on the suggestions from the Commission on Macroeconomics and Health (CMH) (WHO 2001), in which to be considered cost-effective, an intervention has to have a cost-effectiveness ratio of less than three times gross domestic product (GDP) per capita. Below that threshold, WHO-CHOICE considers an intervention to be very cost-effective if each DALY can be averted at a cost of less than GDP per capita (which in the Vietnamese context was VND 13 456 000 or US\$820 in 2007). Since this is a country-specific economic analysis, we report results using local currency units, but make regular conversions to US dollars to help those unfamiliar with Vietnamese Dong.

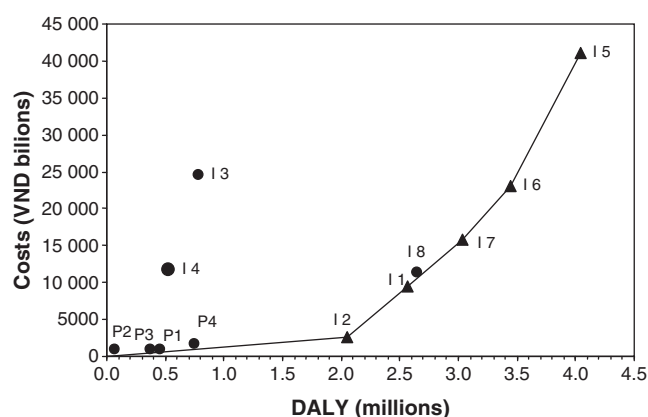


Figure 2 Expansion path for cardiovascular disease interventions.
Note: DALY = disability-adjusted life year.

Uncertainty analysis

We assessed sensitivity analyses on the health effects of various interventions using the lower and upper limits (Table 1) and also the effect of changes in prices (from a half to double the base estimates). We also recalculated the cost-effectiveness ratios without age weight and discounting. Best-case and worst-case scenario analyses were undertaken using lower health effect limits and highest drug prices (worst-case), and upper health effect limits and lowest drug prices (best-case). Finally, we did a probabilistic, multivariate sensitivity analysis using Monte Carlo League (MCLeague) software (another of the WHO-CHOICE tools), assuming a coefficient of variation of 15% on the cost side and 25% on the effectiveness side with 1000 randomly selected sets of variables.

Results

Table 4 represents total annual costs and health effectiveness in terms of age-weighted and discounted DALYs averted, the average cost-effectiveness ratio, incremental cost-effectiveness ratio, and the cost-effectiveness category for all 23 interventions. The least costly interventions are health education programmes through mass media, with a total cost per year of VND 89 billion (US\$0.06 per capita). By contrast, combination drug treatment for individuals with a 5% absolute risk of a cardiovascular event is the most costly intervention (VND 4121 billion/year, equivalent to US\$2.9 per capita). In terms of effectiveness, individual interventions save more DALYs than population-wide interventions, but are more costly. Specifically, population interventions can avert 7000–75 000 DALYs per year when implemented singly or in combination, while individual interventions can save 50 000–400 000 DALYs annually.

According to the Commission on Macroeconomics and Health's classification, all interventions are cost-effective, i.e. below the threshold of three times GDP per capita.

Table 4 Annual cost, effects and cost-effectiveness of interventions

Intervention	Costs per year (VND, billions)	DALYs averted per year	ACER (VND per DALY saved)	ICER (VND per DALY saved)	CMH category*
Media salt campaign	89	45 939	1 945 002	Dominated	Very cost-effective
Media smoking campaign	89	7250	12 324 059	Dominated	Very cost-effective
Media cholesterol campaign	89	36 982	2 416 075	Dominated	Very cost-effective
Mass media combination	167	75 379	2 211 140	Dominated	Very cost-effective
Treatment of SBP >140 mmHg	941	256 559	3 660 315	13 194 115	Very cost-effective
Treatment of SBP >160 mmHg	264	205 329	1 281 596	1 281 596	Very cost-effective
Treatment of cholesterol >5.7 mmol/l	2460	78 179	31 469 764	Dominated	Cost-effective
Treatment of cholesterol >6.2 mmol/l	1174	52 392	22 404 550	Dominated	Cost-effective
Combination treatment (>5% risk)	4121	404 684	10 157 911	30 240 689	Very cost-effective
Combination treatment (>15% risk)	2308	344 868	6 674 633	17 547 288	Very cost-effective
Combination treatment (>25% risk)	1584	303 714	5 201 348	13 585 810	Very cost-effective
Combination treatment (>35% risk)	1129	264 716	4 251 785	Dominated	Very cost-effective

Notes: ACER = average cost-effectiveness ratio; ICER = incremental cost-effectiveness ratio; DALY = disability-adjusted life year; CMH = Commission on Macroeconomics & Health; SBP = systolic blood pressure.

*Very cost-effective: <GDP per capita; Cost-effective: <3 times GDP per capita; Not cost-effective: >3 times GDP per capita. GDP per capita in Vietnam for the year 2007 was VND 13 465 000 (US\$820).

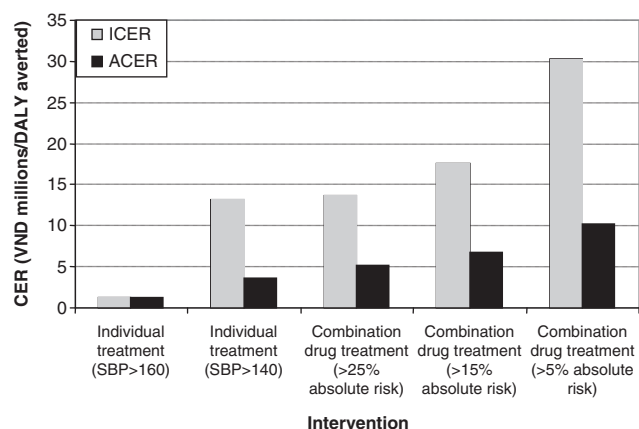


Figure 3 Incremental and average cost-effectiveness ratios for the most cost-effective interventions. *Notes:* CER = cost-effectiveness ratio; ICER = incremental cost-effectiveness ratio; ACER = average cost-effectiveness ratio; DALY = disability-adjusted life year; SBP = systolic blood pressure.

Furthermore, all population interventions implemented either in isolation or in combination are very cost-effective (below the threshold of GDP per capita). Among the population interventions, the health education programme to reduce salt intake is the most cost-effective (VND 1 945 002 or US\$118 per DALY averted), followed by the mass media combination programme (VND 2 211 140 or US\$135 per DALY averted). For individual interventions, results show that both treatment interventions based on elevated levels that aim to reduce cholesterol are less cost-effective when compared with all other measures. Individual treatment for cholesterol >5.7 mmol is least cost-effective (VND 31 469 764 or US\$1916 per DALY averted). Conversely, treatment of systolic blood pressure >160 mmHg is the most cost-effective measure (VND 1 281 596 or US\$78 per DALY averted). With regard to the absolute risk approach, both cost and cost-effectiveness ratios are disproportional to the increase of the risk thresholds.

Figure 2 plots the total costs and effects of all single or combined interventions based on point estimates. The solid line, the expansion path, connects the most cost-effective interventions which would be selected in order to achieve greatest health gain given increasing levels of available resources. The movement would start with individual treatment of systolic blood pressure >160 mmHg (I2) at the budget level of VND 264 billion per year (US\$16.1 million) and then move to individual treatment of systolic blood pressure >140 mmHg (I1). If additional resources became available, combined treatment for those who have an absolute risk of a CVD event in the next 10 years of 25% (I7), 15% (I6) and 5% (I5) should be purchased, respectively. Incremental and average cost-effectiveness ratios for the best individual interventions are shown in Figure 3.

Results of one-way sensitivity analysis and worst/best-case scenario analysis are represented in Table 5. Without age weights and discounting, average cost-effectiveness ratios reduced more than a half, moving almost all interventions to the very-cost effective category, except for individual treatment of cholesterol >5.7 mmol. With lower estimates of effect sizes,

significant increases in average cost-effectiveness ratios of both population and individual interventions to reduce cholesterol were recorded. Notably, health education programme to reduce smoking was very sensitive, moving from very cost-effective to the cost-effective category (VND 12 324 059 per DALY versus VND 29 574 642 per DALY averted). Higher effect sizes did not have much effect on overall average cost-effectiveness ratios, in the sense that they did not move interventions to reduce cholesterol to the very cost-effective category. While no significant changes were recorded when halving the base drug prices, we found that when drug prices were doubled, individual treatment to reduce cholesterol >5.7 is no longer cost-effective, and combination drug treatment for absolute risk of CVD over 5% moves from very cost-effective to the cost-effective category.

Overall, the combination of lower health effects and double drug prices (worst-case) made all interventions least cost-effective. In the worst-case scenario, both individual treatments of cholesterol above 5.7 and 6.2 mmol were not cost-effective (VND 61 554 243 per DALY and VND 43 643 450 per DALY averted, respectively), and media smoking campaign and combination treatment for above 5% absolute risk moved from very cost-effective to cost-effective. On the contrary, in the best-case scenario, all interventions were very cost-effective, except individual treatment of cholesterol >5.7 which still remained in the cost-effective category. Results of sensitivity analyses showed that individual treatment of systolic blood pressure >160 mmHg is always the first choice based on point estimates, and the most commonly chosen expansion path (60%) is the combination of individual treatment of systolic blood pressure >160 mmHg and combination treatment of absolute risks of 25%, 15% and 5%, respectively.

Probabilistic, multivariate sensitivity analysis showed the range of possible point estimates for the expansion path is very wide and there are overlaps between uncertainty intervals (Figure 4). As a result, there is much uncertainty about the choice of interventions. An alternative solution is to use a stochastic league table produced by MCLeague. Figure 5 summarizes the likelihood that a single or combined intervention is selected to maximize health gain at a given available level of budget, creating a stochastic budget expansion path. At the budget level of less than VND 170 billion per year (US\$10.4 million), a health programme to reduce salt intake is chosen in a range of 40–70% probability of being cost-effective. As resources available increase up to VND 250 billion per year (US\$15.2 million), the mass media combination programme is added with a probability ranging from 50–80%. The coverage expands to individual treatment of systolic blood pressure >160 mmHg as the budget increases over VND 270 billion per year.

Discussion

Results of this analysis demonstrate that all population-wide interventions and the majority of individual measures focusing on reducing risk factors of CVD are very cost-effective. Where resources are scarce (less than VND 250 billion per year), a health education programme to reduce salt intake and a combined mass media programme (on salt, tobacco and cholesterol) are the most cost-effective measures and should be purchased first. As more resources are made available,

Table 5 Results of sensitivity analysis on average cost-effectiveness ratio

Intervention	Age weighted, discounted			No age weight, undiscounted			Upper interval of effect size			Lower interval of effect size			Upper interval of effect size			Half drug prices			Double drug prices			Worst-case scenario			Best-case scenario			
	Age weighted, discounted	Discounted	No age weight, undiscounted	Lower interval of effect size	Upper interval of effect size	Half drug prices	Double drug prices	Worst-case scenario	Best-case scenario	Age weighted, discounted	Discounted	No age weight, undiscounted	Lower interval of effect size	Upper interval of effect size	Half drug prices	Double drug prices	Worst-case scenario	Best-case scenario	Age weighted, discounted	Discounted	No age weight, undiscounted	Lower interval of effect size	Upper interval of effect size	Half drug prices	Double drug prices	Worst-case scenario	Best-case scenario	
Media salt campaign	1 945 002	1 360 661	784 687	3 822 742	1 319 691	1 945 002	1 945 002	3 822 742	1 319 691	1 360 661	784 687	3 822 742	1 319 691	1 945 002	1 945 002	3 822 742	1 319 691	1 945 002	1 360 661	784 687	3 822 742	1 319 691	1 945 002	1 945 002	3 822 742	1 319 691	1 945 002	
Media smoking campaign	12 324 059	8 827 551	5 075 610	29 574 642 ^c	7 592 632	12 324 059	12 324 059	29 574 642 ^c	7 592 632	8 827 551	5 075 610	29 574 642 ^c	7 592 632	12 324 059	12 324 059	29 574 642 ^c	7 592 632	12 324 059	8 827 551	5 075 610	29 574 642 ^c	7 592 632	12 324 059	12 324 059	29 574 642 ^c	7 592 632	12 324 059	
Media cholesterol campaign	2 416 075	1 926 370	1 067 278	4 743 342	1 639 674	2 416 075	2 416 075	4 743 342	1 639 674	1 926 370	1 067 278	4 743 342	1 639 674	2 416 075	2 416 075	4 743 342	1 639 674	2 416 075	1 926 370	1 067 278	4 743 342	1 639 674	2 416 075	2 416 075	4 743 342	1 639 674	2 416 075	
Mass media combination	2 211 140	1 677 206	938 869	4 378 467	1 499 729	2 211 140	2 211 140	4 378 467	1 499 729	1 677 206	938 869	4 378 467	1 499 729	2 211 140	2 211 140	4 378 467	1 499 729	2 211 140	1 677 206	938 869	4 378 467	1 499 729	2 211 140	2 211 140	4 378 467	1 499 729	2 211 140	
Treatment of systolic blood pressure > 140 mmHg	3 660 315	2 625 942	1 490 243	4 247 859	3 253 010	2 902 999	2 902 999	4 247 859	3 253 010	2 625 942	1 490 243	4 247 859	3 253 010	2 902 999	2 902 999	4 247 859	3 253 010	2 902 999	2 625 942	1 490 243	4 247 859	3 253 010	2 902 999	2 902 999	4 247 859	3 253 010	2 902 999	
Treatment of systolic blood pressure > 160 mmHg	1 281 596	906 931	517 887	1 478 397	1 145 431	1 031 959	1 031 959	1 478 397	1 145 431	906 931	517 887	1 478 397	1 145 431	1 031 959	1 031 959	1 478 397	1 145 431	1 031 959	906 931	517 887	1 478 397	1 145 431	1 031 959	1 031 959	1 478 397	1 145 431	1 031 959	
Treatment of cholesterol > 5.7 mmol/l	31 469 764 ^c	25 443 195 ^c	14 134 345 ^c	35 838 568 ^c	28 237 731 ^c	20 179 316 ^c	20 179 316 ^c	35 838 568 ^c	28 237 731 ^c	25 443 195 ^c	14 134 345 ^c	35 838 568 ^c	28 237 731 ^c	20 179 316 ^c	20 179 316 ^c	35 838 568 ^c	28 237 731 ^c	20 179 316 ^c	31 469 764 ^c	25 443 195 ^c	14 134 345 ^c	35 838 568 ^c	28 237 731 ^c	20 179 316 ^c	20 179 316 ^c	35 838 568 ^c	28 237 731 ^c	20 179 316 ^c
Treatment of cholesterol > 6.2 mmol/l	22 404 550 ^c	18 453 672 ^c	10 202 427	25 415 809 ^c	20 176 200 ^c	14 370 527 ^c	14 370 527 ^c	25 415 809 ^c	20 176 200 ^c	18 453 672 ^c	10 202 427	25 415 809 ^c	20 176 200 ^c	14 370 527 ^c	14 370 527 ^c	25 415 809 ^c	20 176 200 ^c	14 370 527 ^c	22 404 550 ^c	18 453 672 ^c	10 202 427	25 415 809 ^c	20 176 200 ^c	14 370 527 ^c	14 370 527 ^c	25 415 809 ^c	20 176 200 ^c	14 370 527 ^c
Combination treatment (>5% risk)	10 157 911	7 199 626	4 154 826	11 186 351	9 393 210	6 538 264	6 538 264	11 186 351	9 393 210	7 199 626	4 154 826	11 186 351	9 393 210	6 538 264	6 538 264	11 186 351	9 393 210	6 538 264	10 157 911	7 199 626	4 154 826	11 186 351	9 393 210	6 538 264	6 538 264	11 186 351	9 393 210	6 538 264
Combination treatment (>15% risk)	6 674 633	4 625 969	2 698 540	7 349 062	6 175 706	4 294 317	4 294 317	7 349 062	6 175 706	4 625 969	2 698 540	7 349 062	6 175 706	4 294 317	4 294 317	7 349 062	6 175 706	4 294 317	6 674 633	4 625 969	2 698 540	7 349 062	6 175 706	4 294 317	4 294 317	7 349 062	6 175 706	4 294 317
Combination treatment (>25% risk)	5 201 348	3 567 174	2 090 716	5 727 312	4 814 276	3 345 850	3 345 850	5 727 312	4 814 276	3 567 174	2 090 716	5 727 312	4 814 276	3 345 850	3 345 850	5 727 312	4 814 276	3 345 850	5 201 348	3 567 174	2 090 716	5 727 312	4 814 276	3 345 850	3 345 850	5 727 312	4 814 276	3 345 850
Combination treatment (>35% risk)	4 251 785	2 886 881	1 699 154	4 682 797	3 935 140	2 734 663	2 734 663	4 682 797	3 935 140	2 886 881	1 699 154	4 682 797	3 935 140	2 734 663	2 734 663	4 682 797	3 935 140	2 734 663	4 251 785	2 886 881	1 699 154	4 682 797	3 935 140	2 734 663	2 734 663	4 682 797	3 935 140	2 734 663

Notes: ^cCost-effective intervention; ^{nc}Not cost-effective intervention. The remaining interventions are very cost-effective.

individual treatment of systolic blood pressure > 160 mmHg and combination treatment based on absolute risks of a cardiovascular event of 25%, 15% and 5% in the next 10 years could then be potentially implemented in Vietnam.

Our findings shared many, but not all, similarities with recent cost-effectiveness analyses of interventions to reduce cardiovascular diseases. They are consistent with what were estimated by Murray *et al.* (2003) for the Western Pacific Region B, to which Vietnam belongs, except for interventions to reduce cholesterol (I3–I4). While Murray *et al.* found cholesterol-lowering drug interventions are very cost-effective, we found them merely cost-effective, even not cost-effective when drug prices were doubled. Moreover, our average cost-effectiveness estimates are significantly higher than the regional estimates, due to higher costs and lower health effectiveness. These divergences emphasize the importance of using local and context-specific information to support national priority-setting efforts. Finally, our interventions based on the absolute risk approach using a multi-drug regimen had similar cost-effective results to recent analyses conducted for and in developing countries (Gaziano *et al.* 2006; Rubinstein *et al.* 2009).

Our application of WHO-CHOICE to Vietnam has several caveats. First, although we made use of much local data on costs and epidemiology, no national data on the epidemiology of sodium consumption was available. In the absence of this information, we therefore derived epidemiology and effect estimates from other international studies and then worked with the panel of experts to determine conservative estimates in order to adjust to the context of Vietnam. Secondly, we did not incorporate in the models other benefits, i.e. decrease in the risk of gastric cancer due to reduced salt intake (Tsugane *et al.* 2004; Tsugane 2005), or resistance which may be caused by platelet-active drugs (Patrono *et al.* 2004).

Importantly, this paper has several implications for the policy debate on prevention and control of CVD in Vietnam. First, like other developing countries, Vietnam faces serious financial constraints. A recent report has revealed that, amongst other things, the national budget for health care is unable to meet the people's health care needs, the effectiveness of utilization of the state budget is still limited, and more importantly, resources spent on preventive medicine are far from adequate (MOH 2008). As a result, spending the health budget wisely and efficiently has become increasingly important. Our results provide health policy-makers with more information on what prevention strategies to reduce CVD are cost-effective and how they should be purchased if additional resources are available, thereby increasing efficiency in resource allocation. Specifically, according to the request of the MOH (MOH 2007), the budget allocated for CVD prevention and control was about VND 80 billion in 2008 (US\$4.7 million). At this budget level, the mass media campaign to increase population awareness of the risk factors of CVD, such as salt intake and high cholesterol concentration, should be the first choice. In the long run, ideally cardiovascular health promotion should be a part of the national media strategy. This suggestion was also recommended for the South Asia countries, which, along with Vietnam, are in the second stage of the epidemiologic transition (Nishtar 2002).

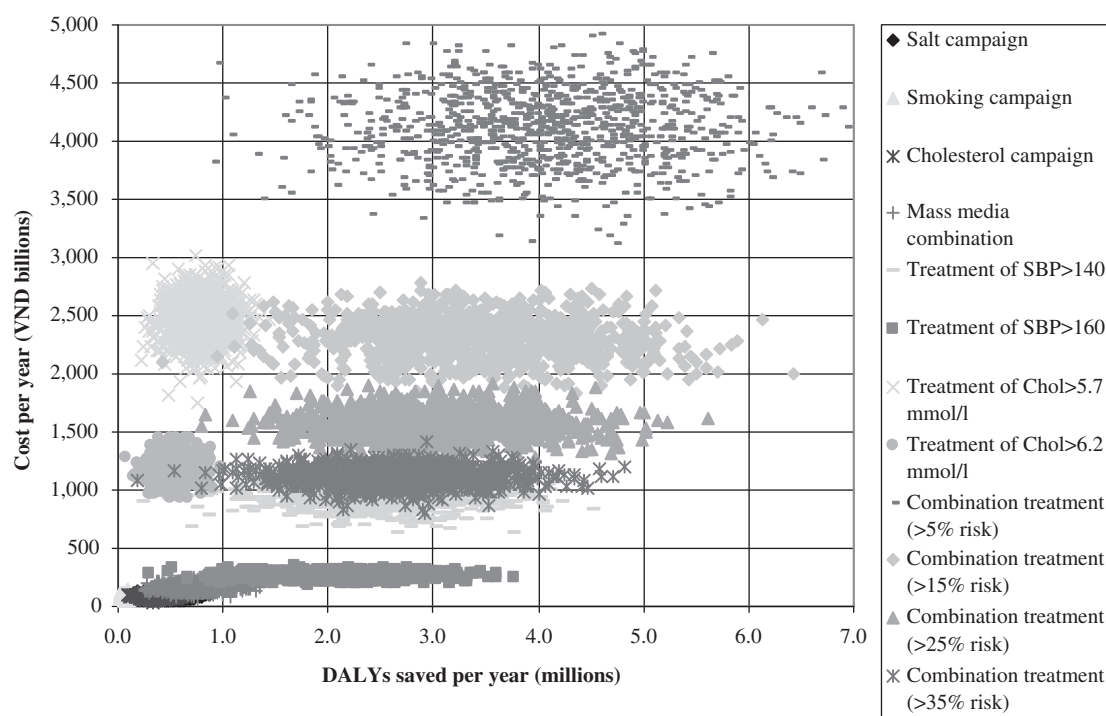


Figure 4 Uncertainty around incremental cost-effective ratios. *Notes:* DALYs = disability-adjusted life years; SBP = systolic blood pressure; Chol = cholesterol.

Secondly, as the budget allocated for the control and prevention of CVD is projected to increase in the coming years, it is recommended that health policy-makers expand the individual prevention treatment of systolic blood pressure, especially for those who have elevated levels over 160 mmHg (which is the most cost-effectiveness intervention). While the extensive development of pharmacies throughout the country would make the scale-up of pharmaceutical interventions more feasible and less costly, and the recent achievement in the expansion of health insurance coverage through several special programmes targeting poor and less affluent people was found to increase access to health care (Ekman *et al.* 2008), there remains some debate around screening for risk factors and adherence to treatment. For example, for those who have high systolic blood pressure, adherence to the life-long treatment regime with two or more antihypertensive agents could be affected by cultural preferences and beliefs (Betancourt *et al.* 1999), clinical inertia (O'Connor 2003), clinician-patient partnership (Barrier *et al.* 2003), and economic barriers (Bovet *et al.* 2002). Therefore, when implemented, these issues should not be neglected. These same issues also apply to the administration of combination pharmacotherapy to those at an absolute risk of experiencing a CVD event in the next 10 years, particularly the latter economic constraint given the higher per capita cost of implementation (e.g. US\$1.13 per capita population for the 25% risk level). This estimate is nearly double that made in a recent modelling study of the financial costs (and health effects) of scaling-up a multi-drug regimen in developing countries, including Viet Nam (US\$0.66 per capita at 2005 price levels; Lim *et al.* 2007).

Thirdly, not only are the suggested prevention measures very cost-effective, but they seem highly feasible in other aspects, particularly from a financial perspective since estimated implementation costs are very low (less than a dollar per capita per year for the most cost-effective strategies). Part of the reason for this financial viability is that all drugs used for treating hypertension and hyperlipidemia are now off-patent, available widely across the country and can therefore be easily scaled up through primary health care or outpatient clinics. Finally, an education programme through mass media to reduce sodium intake is highly recommended by WHO in the recent Forum and Technical Meeting (WHO 2007). In Vietnam, such a measure may prove to be even more effective because the overall knowledge of risk factors for CVD among the Vietnamese people remains relatively low.

Applying WHO-CHOICE using local and context-specific information is a promising approach to improved evidence-based health policy-making in developing countries where data are limited and technical skills are scarce. The following are some lessons learned from our application which other analysts might find useful:

- first, a good panel of local experts representing multiple disciplines plays an important role in guiding interventions and providing insight into how to adjust WHO-CHOICE information for the specific national context;
- second, it is important to fully understand how an intervention pathway reflects the underlying biological process of the disease question and the impact of the intervention (i.e. from the developed intervention pathways, ingredients used in the pathway are documented and then

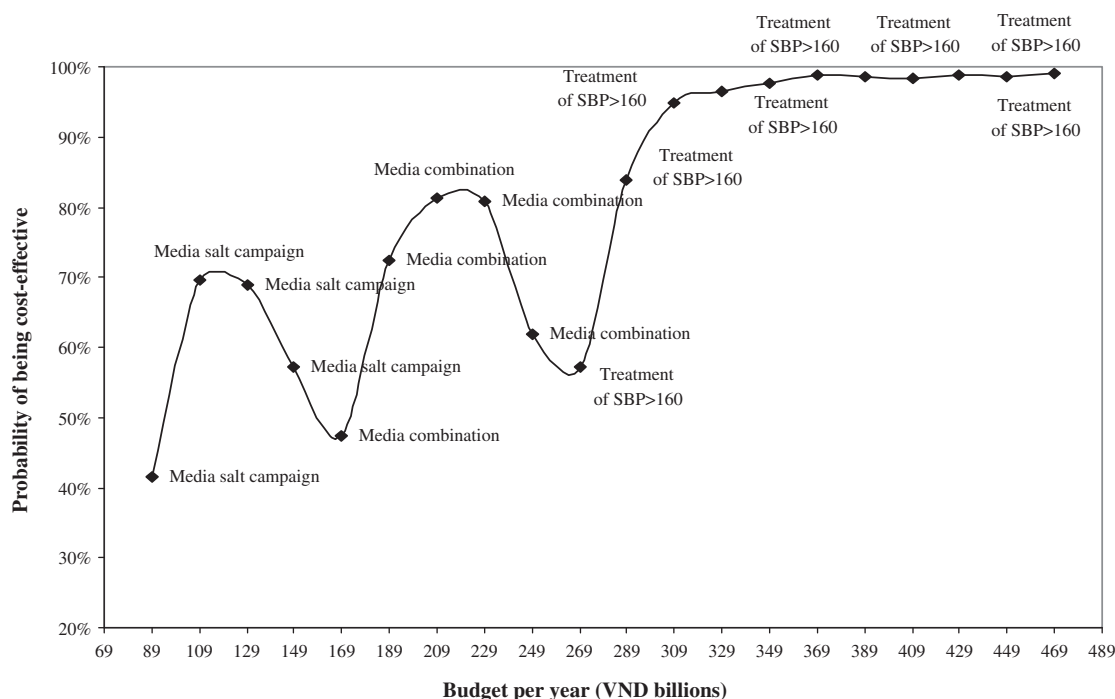


Figure 5 Stochastic budget expansion path *Note:* SBP = systolic blood pressure.

the amount of resources used in the intervention is estimated);

- finally, conducting an economic evaluation using modelling requires that appropriate evidence be elicited from multiple and disparate sources (as opposed to cost-effectiveness analysis undertaken alongside clinical trials). As a rule of thumb, the evidence should not be identified selectively, but derived from the best designed and least biased sources.

Conclusion

As cardiovascular diseases are escalating in Vietnam where resources are very limited, there exists a constant tension over how available resources can be used to best effect. Our analysis brings fresh and practical evidence to policy debates on prevention and control of cardiovascular diseases. Although final decisions may be based on other grounds such as social and geographical equity, cost-effectiveness is among the key inputs and plays a unique role in how to allocate scarce resources. Using the results of this analysis would lead to policy making in Vietnam being driven more by evidence, thereby making decisions more explicit and systematic.

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Disclaimer

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