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Title: Cost-effectiveness of treatment and secondary prevention of acute myocardial infarction in India

Author (1): Itamar Megiddo
megiddo@cddep.org

Affiliation: Center for Disease Dynamics, Economics & Policy
1616 P St. NW, Washington, DC 20036, USA

Author (2): Susmita Chatterjee
susmita.c@phfi.org

Affiliation: Public Health Foundation of India
New Delhi, India

Author (3): Arindam Nandi
nandi@cddep.org

Affiliation: Center for Disease Dynamics, Economics & Policy
1616 P St. NW, Washington, DC 20036, USA

Author (4): Ramanan Laxminarayan
ramanan@cddep.org

Affiliation: Center for Disease Dynamics, Economics & Policy
1616 P St. NW, Washington, DC 20036, USA

Correspondence to: megiddo@cddep.org

Keywords: India; acute myocardial infarction; AMI; coronary heart disease; CHD; cost-effectiveness analysis

Abstract:

Background: Cardiovascular diseases are the single largest cause of death in India, with acute myocardial infarction (AMI), commonly known as heart attack, accounting for a third of all heart disease deaths. Although effective treatment is available for AMI, access to treatment is dictated by cost and ability to pay. With scarce treatment resources, healthcare decisions are guided by local cost-effectiveness, for which country-level data are lacking.

Objectives: We calculate the cost-effectiveness of policies that expand the use of aspirin, injection streptokinase, beta blockers, ACE inhibitors (ACEI), and statins for the treatment and secondary prevention of AMI in India. In addition, we estimate the cost-effectiveness of a hypothetical polypill (combining the aforementioned drugs) for secondary prevention.

Methods: We conduct cost-effectiveness analyses of AMI treatment and secondary prevention for patients with prior coronary heart disease events in India.

Results: Increasing coverage of AMI treatment with aspirin and streptokinase is cost-effective and can avert approximately 335,336 (190,584–502,641) disability-adjusted life years (DALYs) among 30- to 69-year-olds in India. Reducing the time between pain onset and arrival at the hospital could avert an additional 157,000 DALYs. Secondary prevention with aspirin and beta blockers at 80% coverage is highly cost-effective, and the addition of ACEI is also cost-effective. Introducing the polypill dominates a strategy of a four-drug regimen with the aforementioned drugs and statins. The cost-effectiveness ratio of 80% coverage with the polypill is $1,691 ($1,218–$2,407) per DALY averted.

Conclusions: Policies expanding both treatment and preventive therapies are cost-effective compared with the commonly used threshold of gross domestic product (GDP) per capita. Reducing the time to treatment of AMIs could significantly reduce the burden and save lives. Introducing the polypill for secondary prevention would be more effective than providing all of its components separately, even without accounting for the likely increase in treatment adherence.

1. Introduction

Acute myocardial infarction (AMI), commonly known as heart attack, is a major cause of morbidity and mortality in India [1]. Individuals with previous coronary heart disease (CHD) events are at high risk for AMI. There are an estimated 19 million CHD patients aged 30–69 in India,[1] and in 2010 there were 2.1 million deaths from cardio and circulatory disease [2]. Well-established guidelines govern the use of various drugs for the treatment and prevention of AMIs [3]. The Second International Study of Infarct Survival (ISIS-2) found that treating AMI patients with aspirin (an antiplatelet agent) alone or with injection streptokinase (thrombolysis) alone produced a significant reduction in the five-week vascular mortality compared with placebos; the odds reductions were 23% and 25%, respectively, and 42% for combined therapy [4].

In addition to primary treatment and management, secondary prevention of AMIs remains an important strategy to reduce the burden of CHD and AMIs in India. Gaziano et al. 2005 [5,6] find secondary prevention with drugs such as aspirin, beta blockers, ACE inhibitors (ACEI), and statins to be cost-effective for patients in the developing world. These drugs reduce the risk of AMI and lower its case fatality rate. Preventive therapy with aspirin alone, administered to CHD patients, is estimated to reduce the relative risk of an AMI by 34%. The cumulative risk reduction from the combination of all four drugs is approximately 73% [6].

[1] Based on a chort model of CHD, which uses Framingham risk scores on an Indian population data set [19].

The four drugs mentioned above are currently prescribed, albeit at a low rate, in South Asia [7]. The polypill, which combines these drugs into one pill, is new and yet to be introduced. Research has shown that the polypill potentially increases adherence relative to prescription of all pills [8–10].

In this study, we investigate the cost-effectiveness of AMI treatment and prevention using pharmacological interventions. Specifically, we analyze the cost-effectiveness of interventions with aspirin and injection streptokinase for the primary treatment of AMIs, and secondary prevention therapies with aspirin, beta blockers, ACEI, statins, and the hypothetical polypill for patients with prior CHD events. Research has been done in the developing world and in South Asia as a region [5,6]. This analysis focuses on India, which accounts for approximately 60% of heart disease in the world [11]. Disease epidemiology in India is different in several respects: 54% of CHD deaths in India occur before age 70 [2], whereas the proportion is 22% in the West [12], 38% in Iran and Sri Lanka, and 34% in China [13]. We follow the World Health Organization guidelines for calculating the cost-effectiveness ratio (CER) as the incremental cost per disability-adjusted life year (DALY) averted by an intervention relative to a baseline scenario of current prescription rates in India. We consider the costs from the perspectives of both the health sector and the individual patient and report commonly used thresholds of “cost-effective” and “very cost-effective,” which compare the CER with per capita gross domestic product (GDP).

2. Methods

Modeling approach

We assess the cost-effectiveness of AMI treatment and secondary prevention by conducting a cost-effectiveness analysis (CEA). Our analysis follows the World Health Organization (WHO) guidelines for calculating the CER of each intervention as the cost per DALY averted by the intervention relative to the null scenario, in which no effective AMI intervention is administered [14]. The disease burden in the baseline scenario is calculated by accounting for the effectiveness of the current treatment and prevention therapy prescription regimens. We incorporate morbidity reductions (years of life lost to disability, or YLD) and mortality reductions (years of life lost, or YLL) from the intervention drugs relative to the baseline. The CER is the ratio of the total cost of the intervention, both to the health sector and to the patient, and the sum of YLL and YLD averted by the intervention.

YLL is calculated based on the age at death, remaining life expectancy, and a 3% discount rate. Life expectancy for CHD patients is estimated based on WHO life tables, the mortality rate from the disease, and the secondary prevention treatment regimen offered. Higher levels of preventive therapy prescription increase the life expectancy of the patients. Averted YLLs are based on the deaths that would occur in the baseline scenario, the level of intervention coverage, and the effectiveness of the treatment. Averted YLDs are the product of the disease duration, disability weight, incidence of the condition, and coverage and effectiveness of the intervention. For secondary prevention, we assume that patients are on the treatment regimen for the rest of their lives (remaining life expectancy). The disability weight for AMIs is 0.437 (range 0.405–0.477) based on risk factors and the global burden of disease [15].

We report the commonly used thresholds of "cost-effective" and "very cost-effective," which compare the CER with per capita GDP. A "very cost-effective" intervention is assumed to have a CER less than per capita GDP per DALY averted, and a "cost-effective" intervention has a CER of less than three times per capita GDP per DALY averted [14]. CERs are produced for all Indians aged 30–69 years. We use uniform age weights that value an extra year of life equally, regardless of the age of the recipient.

Intervention options and strategies

AMI treatment interventions

We separately analyze ST-segment elevation myocardial infarction (STEMI) and non-ST segment elevation myocardial infarction (NSTEMI). In a STEMI the heart muscles being supplied by the affected artery die, whereas in an NSTEMI, only a portion of the heart muscles being supplied by the affected artery die. Treatment of AMI involves medical therapies that restore blood flow (using antiplatelet agents), dissolve the thrombus that is occluding the arterial lumen (thrombolysis), or reduce myocardial oxygen demand and fatal arrhythmias (beta blockers). Although immediate treatment for STEMI should involve the antiplatelet agents and thrombolysis, invasive intervention (e.g., cardiac catheterization and angioplasty) is also an option [12].

In this study, we present two primary treatment scenarios for AMI patients and calculate the CERs of each. In intervention scenario 1, patients are treated with aspirin alone (325 mg initial

dose and subsequently 75 mg doses once daily); in scenario 2, patients are treated with aspirin and injection streptokinase (one dose at 1.5 mU) [16]; only STEMI patients are treated with the injection. In both cases we assume patients are administered treatment within 24 hours of an AMI.

Prevention interventions

Patients with previous CHD events are at a high risk of AMI. Systematically identifying them and offering them intensive preventive treatment could prevent many vascular events and deaths. Thus, secondary prevention is recognized as a public health strategy to reduce disease burden [17]. Here, we calculate the CEA of 1) aspirin (75 mg once daily); 2) aspirin and beta blockers (75 mg once daily and 50 mg twice daily, respectively); 3) aspirin, beta blockers, and ACEI (75 mg once daily, 50 mg twice daily, and 5 mg once daily, respectively); 4) aspirin, beta blockers, ACEI, and statin (75 mg once daily, 50 mg twice daily, 5 mg once daily, and 10 mg once daily, respectively); and 5) a hypothetical polypill to be taken once daily consisting of aspirin (75 mg), statin (10 mg), beta blocker (50 mg), and ACEI (5 mg). All these drug combinations are to be taken indefinitely (based on calculated life expectancy of the CHD patients).

Data sources, assumptions, and calculations

Number of AMI cases and prevalence of CHD

No data on the number of AMI patients in India are currently available. We estimated the risk of AMI from existing data in a two-step process. First, we calculated the prevalence of CHD. Existing measures of CHD prevalence differ substantially. The National Commission on

Macroeconomics and Health (NCMH) background papers predicted 42.5 million CHD patients aged 30–69 [16]. Based on that, in a rough approximation[2] of the death rate of CHD patients (from CHD), the 2010 Global Burden of Disease Study (GBD) 2010 predicted the percentage of deaths [2] as 1.4%. Based on a meta-analysis of Indian district surveys updated to 2013, Basu et al. 2013 [18] assume that approximately 21.9 million Indians aged 30–69 have CHD. Given the number of deaths they predict, the rough death rate is 3.3%.

We calculated the prevalence of CHD using 10-year risk scores of CHD event incidence based on data from Jeemon et al. (2011) [19]. We then estimated the prevalence for four age groups between 30 and 69 years using a cohort ordinary differential equation model. Because of the large variance in estimated prevalence across studies, we used a wide range for CHD incidence in our sensitivity analysis.

At the second step, the risk of AMIs [20] was back calculated to incorporate current secondary prevention prescriptions in India [7]. The details of the model parameters are presented in Table 1.

Death rate

Thirty-day mortality after an AMI, even with effective treatment, is about 33%, with roughly half the deaths occurring before the patient reaches the hospital [12]. To calculate the cost-effectiveness of AMI treatment interventions, we used the death rate for hospitalized STEMI (8.6%) and NSTEMI (3.8%) patients as reported in the prospective registry study (CREATE)

[2] The approximation is a simple division of deaths by prevalence. Since the death rate affects prevalence, the result is a slight underestimation.

119 carried out in India [11]. For the analysis of the prevention therapies for CHD patients [20], the
120 annual death rate incorporating the current secondary prevention prescriptions in India was
121 7.5% [7]. The rough estimates of the death rates calculated from the GBD and NMCH studies
122 are lower than our rates. We used a wide range in our sensitivity analysis to incorporate the
123 uncertainty.

124 *Coverage of drugs*

125 Current drug coverage data for AMI treatment were taken from the results of the CREATE study
126 [11]. We assumed that the coverage rates of secondary prevention drugs in India were
127 equivalent to the South Asian PURE study estimates [7]. We also assumed that the drugs were
128 prescribed as combination therapies as follows: since statins have the lowest prevalence, the
129 4.8% of patients who take them also take all other drugs; next come ACEIs, with a prevalence of
130 6.4%, and therefore, 1.6% take all drugs but statins; and similarly with aspirin and beta blockers
131 (Table 1). The coverage of the polypill, which is unavailable in India, was set to zero. Compared
132 with the baseline rates mentioned above, we analyze new health policy scenarios that would
133 lead to a 95% coverage for AMI treatment with aspirin, and 80% intervention coverage for all
134 other scenarios.

135 *Effectiveness of drugs*

136 The INTERHEART study confirmed that risk factors for AMI are the same globally regardless of
137 income levels [21]. Therefore, we assume that interventions have the same effect (relative risk
138 reduction) in developed and developing countries.

Effectiveness of aspirin, and aspirin with injection streptokinase, was calculated from the results of the ISIS-2 study [4]. Effectiveness of the sets of drug combinations used for secondary prevention was calculated from Gaziano et al. 2006 [6], and effectiveness of the hypothetical polypill was taken from the Indian polycap study [21].

Since no interactions between treatment effects were observed in trials, a multiplicative scale was used to calculate the cumulative risk reduction of different drug combinations used for secondary prevention [22]. For example, two interventions that each reduced the risk of any vascular event by 30% would be expected to have a 51% combined relative risk reduction [1-(0.70*0.70)].

Cost components

We considered the costs of the interventions from the perspectives of both the health sector and the patient. Primary AMI treatment intervention costs included the cost of drugs, laboratory tests, and inpatient stay at a secondary hospital. Drug costs were taken from the Current Index of Medical Specialties India website [23]. The laboratory tests required to diagnose and treat AMI patients were identified from the NCMH background papers. Laboratory tests needed during a hospital stay included one lipid profile, one chest x-ray, five ECGs, two echocardiographies, a liver function test, a renal function test, a haemogram, three tests for cardiac enzymes, and one test for blood glucose. Unit cost data for these tests were not available for India; we therefore used the “standard unit cost” (at 2009 Thai Baht) calculated by Riewpaiboon et al. (2011) [24] for Thailand’s Health Intervention and Technology Assessment Program. Three district hospitals and three provincial hospitals that met the

established efficiency criteria (more than 80% inpatient bed occupancy) were selected for the unit cost calculation of laboratory tests. The unit test costs were calculated using both standard costing and relative value unit (RVU) methods [25,26]. The unit cost of inpatient stay was taken from WHO estimates for district hospitals in India (at 2005 prices) [27]. This cost, specific to public district hospitals with an occupancy rate of 80%, includes personnel, capital, and food costs but excludes costs of drugs and diagnostic tests. All costs were adjusted using the consumer price index, and the final estimate was presented in 2010 US dollars.

Secondary prevention costs included outpatient visits, drugs, and the aforementioned costs of AMIs. WHO's estimate was used for the unit cost per outpatient visit, the number of times that patients needed to visit the hospital per year and the number of laboratory tests they received per year were taken from the NCMH background papers [16]. The cost of both treatment and secondary prevention interventions exclude travel and missed days of work to obtain treatment. The details of cost components are presented in Table 1.

Sensitivity analysis

To assess the uncertainty in the model and the robustness of the results, we conducted sensitivity analysis using a Latin hypercube sampling (LHS) technique. The distribution parameters of each variable used in the analysis are listed in Table 1. They are based on the upper and lower limits reported in previously published work, where available. Where limits are not available, we constructed intervals at 85% and 115% of the values reported. The exceptions are the CHD incidence and death rates, where the intervals were set to 50% and 150%.

3. Results

CHD prevalence

Based on the cohort model, approximately 19 million 30- to 69-year-old individuals in India have had prior CHD events. We have wide confidence intervals in our sensitivity analysis (13.4 million–27.5 million) because of the wide estimates of incidence and CHD death rates. (Table 2).

AMI treatment interventions

Table 3 provides CEA results with 95% confidence intervals from the LHS sensitivity analysis. The incremental cost-effectiveness ratio (ICER) of increasing aspirin AMI treatment coverage at hospitals from the baseline (80%) to the intervention (95%) scenario is only $0.49 ($0.28–0.90) per DALY averted. Increasing coverage of injection streptokinase from 22.5% to 80% of STEMI patients (in addition to the aspirin intervention) averts an additional 38,102 (15,304–82,559) DALYs in the Indian population and the ICER is $615 ($350–1,209) per additional DALY averted, respectively. Administering both treatments consistently within four hours of the AMI averts an additional 157,267 DALYs (not taking into account reduced prehospital deaths).

Prevention interventions

The life expectancy without preventive treatment was approximately 9.7 (95% CI of 8.2–11.4 in the sensitivity analysis) years for 30- to 39-year-olds, 9.2 years (7.7–10.6) for 40- to 49-year-olds, 8.5 years (7.1–9.8) for 50- to 59-year-olds, and 7.4 years (6.3–8.5) for 60- to 69-year-olds. Preventive interventions can extend life expectancy by up to 5.2 (1–9.6) years, 4.5 (0.8–8.3) years, 3.7 (0.5–6.8) years, and 2.7 (0–5.5) years in the respective age groups.

The incremental cost-effectiveness and DALYs averted of the four preventive combination therapies are 1) aspirin, $265 ($145–572) per DALY averted, with almost 1.4 million DALYs averted from the baseline; 2) aspirin and beta blockers, $1,741 ($977–4,275) per DALY averted, with more than 2 million additional DALYs averted; 3) aspirin, beta blockers, and ACEI, $2,773 ($1,378–10,207) per DALY averted, with almost 1.4 million additional DALYs averted; and 4) aspirin, beta blockers, ACEI, and statins, $6,447 ($3,416–18,937) per DALY averted, with approximately 1.8 million additional DALYs averted. Provision of the polypill to 80% of CHD patients averts approximately 7.3 million DALYs in the Indian population (from the baseline) with a CER incremental to the baseline of $1,691 ($908–4,100) per DALY averted. The polypill intervention strongly dominates the intervention of the combination of the four preventive drugs. Results from the LHS sensitivity analysis provide a similar outcome, maintaining the same CER rank; in a few (parameter combination) scenarios, the DALYs averted from the four combination-therapy interventions are higher than for the polypill intervention, though the CER rank remains the same.

4. Discussion

AMI treatment

Treatment in hospital with aspirin is already relatively high in India, and thrombolysis (injection streptokinase) is more common than in other developing countries [28]. AMI management with thrombolysis is also higher than in developed countries, where there is a higher prevalence of primary angioplasty [11]. Angioplasty has advantages over thrombolysis [29,30] and is

sometimes used as the first-line treatment for AMIs [30]. However, only an estimated 7.5% of AMIs are treated with angioplasty in India, and the costs are extremely high for patients, who often (77.3% of the time) pay out of pocket [11]. Our analyses have shown that the AMI treatment interventions, expanding provision of both aspirin and streptokinase, are highly cost-effective. The case remains when conducting a sensitivity analysis on the parameters used in the model.

However, the problems in the Indian AMI management infrastructure begin at the lack of availability of timely treatment. Prehospital paramedical support and ambulance services are used by only 5% of suspected AMI patients in India. Other patients use taxi, auto-rickshaw, or private transport (62.7%) or public transport (32.2%) [11]. For India, the CREATE study estimated that the mean time of arrival at the hospital from pain onset was 300 minutes (61.9% arrived more than four hours from pain onset), relative to developed countries, where mean times ranged from 140 to 170 minutes [11]. In China, research has found time from pain onset to arrival was 150 minutes for males and 270 minutes for females (30 minutes of each was for transportation) [31]. Another study found that 39.5% of Chinese AMI patients called emergency medical services (EMS) at pain onset, with a median prehospital delay of 110 minutes (the median for self-transported patients was 143 minutes) [32]. Moreover, use of EMS can reduce the time from arrival at the hospital to treatment. The delay may partially explain the higher AMI NSTEMI death rates in India than in China [20].

Reducing the time from pain onset to treatment to less than four hours consistently can save additional lives and reduce the burden. However, such an intervention would require education

241 of the public and interventions to increase transportation and/or administer thrombolysis
242 before hospital admission. Encouraging prompt hospitalization and starting treatment with
243 aspirin at home or in the ambulance (while also increasing EMS) or emergency room before
244 transfer to the coronary care unit are therefore recommended. However, injection
245 streptokinase produces some adverse side effects during and after infusion and should be
246 administered under careful monitoring [4].

247 **Prevention**

248 The variation in the use of AMI drugs across the globe is extremely high. CHD patients in South
249 Asia use secondary prevention therapy, such as antiplatelet drugs (11.6%) and ACEIs (6.4%), at a
250 slightly lower rate than in China (15.5% and 7.8%, respectively) and Malaysia (14.9% and 12.8%,
251 respectively). Beta blockers and statins are used at a lower rate in China (6.8% and 2%,
252 respectively) than in South Asia (11.9% and 4.8%, respectively) but at a higher rate in Malaysia
253 (12.5% and 15.9%, respectively). Prescription is much higher in North America and Europe
254 (range of 45.4%–56.7% for the four drugs), South America (19%–40.2%), and the Middle-East
255 (26.2%–52.7%) [7].

256 Much of the variation in drug use is explained by a strong correlation with countries' health
257 expenditures per head and with GDP. The discrepancy is clearest in the case of statins, which
258 are more expensive and are used relatively infrequently in South Asia and China but are the
259 most-used drug in high-income countries (70.9%) [7]. The culprit for the low rates in India may
260 again be the high percentage of out-of-pocket expenditure in the health care system. However,
261 even use of aspirin, an inexpensive drug, is low.

Preventive therapy interventions have a higher cost because of the need to target a far greater population than the population for AMIs in the hospital. In India, where the onset of cardiovascular diseases is 5–10 years earlier in life than in Western populations [33], that population is especially large. However, for the same reasons, the number of DALYs averted and burden alleviated by interventions with preventive strategies is very high. Interventions 1 (aspirin) and 2 (both aspirin and beta blockers), assuming 80% coverage in both, are very cost-effective according to the GDP per capita threshold. If the prevalence of CHDs is extremely high, intervention 2 is no longer very cost-effective but remains cost-effective. Intervention 3 (incrementally adding ACEI to intervention 2, also at 80% coverage) remains cost-effective and alleviates the burden further.

One possible barrier to secondary prevention is adherence. The polypill has the advantage of being one pill instead of four, which could contribute to more widespread use and greater adherence [8–10]—something not taken into account in this analysis. Except for rare (parameter combination) cases, provision of the polypill to 80% of prior CHD event cases dominated intervention 4, which incrementally adds statins to aspirin, beta blockers, and ACEI. The polypill intervention remains cost-effective when CHD prevalence is extremely high. It should be noted that the only polypill trial carried out in India (TIPS) focused on middle-aged individuals without cardiovascular diseases; it was used as a primary prevention intervention. Wald and Law 2003 found that the polypill strategy could largely prevent heart attacks if taken by everyone with existing cardiovascular disease [34].

Secondary prevention for CHD patients can be cost-effective, saves lives, and increases the life expectancy of patients. However, the barriers to increased secondary prevention are not immediately clear. There is a paucity of national data in India. Most developed countries have established registries documenting AMI intervention. In the developing world most of the data come from small studies. Nationally representative data are important for research, for formulating guidelines, and for devising strategies of adherence to those guidelines.

5. Conclusion

Current prescription rates for secondary prevention drugs of patients with prior CHD events in India are very low. Given the favorable cost-effectiveness of their incremental use, there should be a focus on widespread increase in the regimen of preventive drugs. Increasing primary treatment and reducing the time from pain onset to treatment can further alleviate the burden. Although there are some risks involved in using AMI treatment and secondary prevention medications (e.g., intracranial bleeding increases by nearly 25% with the use of antiplatelet agents, though in absolute terms that is 1–2 cases per 1,0000 patients treated) [12], which we did not consider, the benefits of these drugs far outweigh the risks.

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Table 1. Description of model parameters

Parameter	Value	Sensitivity analysis intervals	Source
Population distribution			World Bank population projection tables
30–39	177,436,000	(150,820,600–204,051,400)	
40–49	137,941,000	(117,249,850–158,632,150)	
50–59	102,481,000	(87,108,850–117,853,150)	
60–69	56,377,000	(47,920,450–64,833,550)	
CHD Incidence per 100,000			Jeemon et al. (2011)
30–39	175	(88–263)	
40–49	590	(295–885)	
50–59	1,018	(509–1,527)	
60–69	1,583	(792–2,375)	
Life expectancy			WHO life table & World Bank population projection tables
30–39	39.57	(33.64–45.51)	
40–49	30.80	(26.18–35.42)	
50–59	22.56	(19.17–25.94)	
60–69	15.32	(13.03–17.62)	
AMI probability with previous CHD events	0.053	(0.047–0.061)	Prabhakaran et al. (2005)
Percentage of STEMI among AMI patients			Xavier et al. (2008)
30–49	68.0%	(%57.8–%78.2)	
50–69	58.0%	(%49.3–%66.7)	
Percentage of AMI patients dying before hospital	16.5%	(%14.0–%19.0)	Gaziano et al. (2006)

30 day AMI mortality rate			Xavier et al. (2008)
STEMI	0.086	(0.073–0.099)	
NSTEMI	0.038	(0.032–0.044)	
CHD yearly death rate	0.079	(0.039–0.118)	Prabhakaran et al. (2005)
Baseline coverage of drugs			
Treatment of AMI			
Aspirin	21.5%	(%18.3–%24.7)	Xavier et al. (2008)
Aspirin + injection streptokinase	58.5%	(%49.7–%67.3)	
Secondary prevention of AMI			
Aspirin	0.0%	(%0.0–%0.1)	Yusuf et al. (2011)
Beta blocker	0.3%	(%0.26–%0.35)	
Aspirin + beta blocker	5.3%	(%4.5–%6.1)	
Aspirin + beta blocker + ACEI	1.6%	(%1.4–%1.8)	
Aspirin + beta blocker + ACEI + statin	4.8%	(%4.1–%5.5)	
Poplypill	0.0%		
Drug efficacy (attributable risk)			
Treatment of AMI			
Aspirin	0.230	(0.150–0.300)	ISIS (1988)
Aspirin + injection streptokinase	0.420	(0.340–0.500)	
Secondary prevention of AMI (Cumulative relative risk)			
Aspirin	0.340	(0.280–0.400)	Gaziano et al. (2006)
Beta blocker	0.270	(0.130–0.250)	
ACEI	0.200	(0.100–0.300)	
statin	0.290	(0.180–0.380)	
Secondary prevention of death (Cumulative relative risk)			
Aspirin	0.150	(0.110–0.190)	Gaziano et al. (2006)
Beta blocker	0.230	(0.150–0.310)	

ACEI	0.160	(0.050–0.250)	
statin	0.220	(0.130–0.310)	
Polypill prevention of CHD events	0.620	(0.527–0.713)	Yusuf et al. (2009)
Costs ($)			
AMI treatment			
Lab costs	304.92	(259.18–350.66)	Riewpaiboon (2010)
Inpatient costs	118.29	(100.55–136.04)	
Aspirin	0.11	(0.10–0.13)	
Aspirin + injection streptokinase	55.05	(46.79–63.30)	
Secondary prevention (DDD)			www.mims.com
Aspirin	0.008	(0.007–0.009)	
Beta blocker	0.071	(0.061–0.082)	
ACEI	0.062	(0.053–0.072)	
statin	0.179	(0.152–0.206)	
Polypill	0.209	(0.178–0.240)	
Disability weight AMI	0.437	(0.405–0.477)	Lopez et al. (2006)
Discount rate	0.030		
Days of disability for AMI patients	30	(26–35)	NCMH (2005)

Sensitivity analysis ranges are based on ranges provided in published works where available. Where not available, a range of 85%–115% of the value was used.

Table 2. CHD cohort model results

Variable	Prevalence	Total
CHD 30–39	0.79% (0.50%–1.11%)	1,400,561 (813,540–2,128,650)
CHD 40–49	2.97% (1.85%–4.44%)	4,123,475 (2,424,478–6,247,783)
CHD 50–59	6.68% (3.92%–9.69%)	6,906,165 (4,276,610–10,279,880)
CHD 60–69	11.50% (6.96%–16.86%)	6,545,696 (3,815,059–9,552,719)
Total		**18,975,896 (13,365,795–27,492,236)**

Results are based on a cohort model using CHD incidence rates and mortality. 95% CIs from sensitivity analysis in brackets.

Table 3. Cost-effectiveness analysis results

Intervention	DALYs averted (from baseline)	Cost-effectiveness ratio	Sequentially incremental (to baseline) cost-effectiveness ratio	Cost-effectiveness
AMI treatment				
Aspirin (to baseline)	297,234 (148,887–553,324)	$98.59 (68.93–156.83)	$0.49 (0.28–0.90)	Very cost-effective
Asprin + injection streptokinase	335,336 (164,191–635,922)	$127.17 (89.72–201.407)	$614.73 (349.96–1208.50)	Very cost-effective
AMI prevention				
Aspirin (to baseline)	1,375,465 (707,199–2,146,599)	$1,011.11 (622.68–1,954.504)	$265.18 (145.25–572.45)	Very cost-effective
Aspirin + beta blockers	3,456,530 (1,772,641–5,610,314)	$1,381.26 (844.47–2,964.374)	$1,740.69 (976.72–4,276.22)	Very cost-effective
Aspirin + beta blockers + ACEI	4,844,229 (2,167,909–7,986,906)	$1,732.98 (1,060.58–3,760.177)	$2,772.60 (1,378.21–10,207.01)	Cost-effective
Aspirin + beta blockers + ACEI + statin	6,699,214 (3,039,122–10,927,104)	$2,923.48 (1,848.72–6,092.639)	$6,446.57 (3,415.78–18,936.81)	Dominated by polypill intervention
Polypill (to baseline)	7,322,859 (4,334,065–10,723,581)	$1,764.92 (975.05–4,117.893)	$1,691.24 (907.71–4,100.11)	Cost-effective

95% CIs from sensitivity analysis in brackets. The thresholds of “cost-effective” and “very cost-effective” compare the CER with per capita GDP. A very cost-effective intervention is assumed to have a CER less than per capita (GDP) per DALY averted, and a cost-effective intervention has a CER of less than three times per capita GDP [14] per DALY averted.