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The health effects and costs of the interventions to control cardiovascular disease in Kyrgyzstan

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Summary

Cardiovascular disease (CVD) is one of the leading causes of morbidity and mortality in the world. About 80% of the global burden of CVD-related deaths occurs in low- and middle-income countries. The disease burden in Kyrgyzstan shows a similar picture as CVD is responsible for the largest share of morbidity and mortality and is responsible for more than half (54%) of the overall mortality (2003)[1]. It is particularly concerning from an economic and social perspective that for the last ten years, the CVD disease burden has been increasingly shifting to younger age groups. The mortality rate from the CVD among 30-39 year old population increased from 47.4 per 100,000 in 1991 to 56.1 in 2006, an 18.3% increase. Similar tendency is traced among the age group of 40-49 and 50-59 years old. As a result of the worsening cardiovascular health of working age adults, families are losing their breadwinners due to death and early disability. CVD is the primary reason for early disablement in the adult population, amounting to 17.4% and exceeding similar indices for other diseases[2].

Due to the economic and social significance of this disease burden, CVD has been identified as one of the priority programmes in the National Healthcare Reform Programme "Manas Taalimi" (2006-2010). In the early phase, a number of studies were conducted to allow effective development of policies and actions to reduce the CVD disease burden. The studies led to the development of the "CVD Control National Programme (2009-2013)" in 2008 aiming to reduce CVD mortality and morbidity through a complex approach at several levels of care (population, primary health care, secondary and tertiary).

The purpose of this study is to contribute to the prioritization of the interventions included in the National Programme by identifying the set of interventions that would produce the greatest health gain for available resources. Accordingly, the study estimates the health effects, costs and cost-effectiveness of the interventions and ranks them by these criteria.

To accomplish this, the study is based on **cost-effectiveness analysis** for three events: acute myocardial infarction (AMI); stroke and congestive heart failure (CHF) at the primary and hospital levels. We use the WHO CHOICE methodology (which is an acronym of **CHO**osing **I**nterventions that are **C**ost-**E**ffective). CHOICE is a tool that aims to provide evidence for selecting interventions which improve the performance of the health systems by maximizing health for the available resources. This tool was contextualized to the Kyrgyz context by getting the best available local data on demography, level of risk factors, current treatment coverage, resource utilization rates and costs of care for specified disorders. We selected 29 single interventions from the National Programme, plus a further 8 plausible combination strategies, so in total we evaluated 37 different interventions. The interventions include health promotion activities as well as treatment activities.

The findings show that the top seven most cost-effective interventions in the CVD strategy are:

- educating people about the benefits of quitting smoking, reducing blood cholesterol level and daily salt intake through mass media campaigns;
- providing appropriate hypertension-lowering drug treatment to individuals whose systolic blood pressure is over 160;
- providing aspirin during the acute phase of acute myocardial infarction (AMI) ;
- providing beta blockers, aspirin and ACE inhibitors during post-acute phase of AMI;
- providing aspirin during the post-acute phase of ischemic stroke;
- providing diuretics for congestive heart failure (CHF)
- providing cardiac rehabilitation for all three conditions;

In addition to these findings, our analysis revealed further factors hindering the reduction in the cardiovascular disease burden. First, activities that are cost-effective in other countries turned out to be not cost-effective in the Kyrgyz context. For example, the use of statins for AMI events

[1] WHO "Highlights on health in Kyrgyztan 2005", 2006
[2] RMMC, 2006 "Population's Health and healthcare Institutions' Activities in KR"

is not cost-effective based on the results of our study, based on the finding that the price of statins is extremely high (37.5 soms per dose, compared to the equivalent of 1.38 Euro (73.14 som in Finland. Second, to treat AMI during the acute phase with combination of Aspirin and Anti-coagulant therapy is highly cost–effective in the Kyrgyz context; however there is no well documented international study of any additional impact over and above the use of Aspirin administered alone. Though, it's commonly used among doctors in Kyrgyzstan - some of them are still committed to methods that had been introduced earlier than the other methods such as Aspirin, Beta-blockers etc.

On the basis of the findings of the study, we recommend focusing on these seven interventions in the first phase of implementing the National Programme as well as taking measures to make medicines for the treatment of these conditions affordable.

The first section of this report provides an overview of the CVD epidemiological situation in Kyrgyzstan and presents the rationale for this study. The objective of cost-effectiveness analysis is described in the second section and the WHO CHOICE methodology is explained in detail in the third section. The methodology includes a description of assessed interventions, as well as explanation of how effectiveness and costs were estimated. The data sources are presented in the fourth section. The results of the study and recommendations/conclusions are discussed in the fifth and sixth sections respectively.

1. Background

At the beginning of the 20th century CVD was responsible for less than 10 percent of all deaths worldwide but by 2001 that figure was 30 percent. Murray and Lopez[3] predicted that CVD will be the leading cause of death and disability worldwide by 2020, mainly because it will increase in low- and middle-income countries. Thus, by 2001, CVD had become the leading cause of death in the developing world, as it has been in the developed world since the mid 1900s[4]. The CVD-related death rate in high-income countries as a whole is 320 per 100,000 population, but in the specific region of Europe and Central Asia, the rate is more than doubles (690 CVD deaths per 100,000 population). Ischemic heart disease (IHD), stroke and congestive heart failure (CHF) account for at least 80 percent of the burden of CVD in all income regions, which share many of the same common risk factors; accordingly, similar interventions are appropriate.

The disease burden in Kyrgyzstan shows a similar picture, CVD takes the first place in the structure of general mortality of the population in Kyrgyzstan and makes almost the half (47.5%) of all annual mortality cases. In 1999 the CVD-related mortality rate was 77 cases per 100,000 population and in 2003 it increased to 86 per 100,000[5]. The mortality indicator from acute myocardial infarction (AMI) is 389 cases per 100,000 population (WHO, 2004). As regard to stroke-related deaths Kyrgyzstan is the leading country among the CIS countries, mortality indicator is 261 cases per 100,000 population (WHO, 2004). In the last decade a tendency shows that mortality rate from CVD in the age of 30-39 has increased from 47.4 per 100,000 in 1991 to 56.1 in 2006, an 18.3% increase. Similar tendency is traced among the age group of 40-49 and 50-59 years old. As a result of the worsening cardiovascular health of working age adults, families are losing their breadwinners due to death and early disability. CVD is the primary reason for early disablement in the adult population, amounting to 17.4% and exceeding similar indices for other diseases[6].

Due to the high burden of this disease, CVD is identified as one of the four priority programmes in the national healthcare reform programme "Manas Taalimi" (2008-2010). In 2007 the Health Policy Analysis Unit (HPAU) (Center for Health System Development–CHSD) conducted a

[3]Murray C, Lopez A., The Global Burden of Disease. Geneva, WHO; Harvard School of Public Health; WB, 1996
[4]Mathers C, Lopez A, and Murray C, 2006, "The Burden of Disease and Mortality by Condition: Data, Methods, and Results for 2001." *Global Burden of Disease and Risk Factors ,ed.* 45-93. New York: Oxford University Press, 2006
[5] WHO, "Health for all", 2004
[6] RMMC, 2006 "Population's Health and healthcare Institutions' Activities in KR"

comprehensive study on the "Quality of preventive and treatment services for AMI and Stroke in the Kyrgyz Republic"[7]. The main purpose of that study was to conduct a comprehensive assessment of the quality of treatment and prevention of CVD in Kyrgyzstan in order to identify the main areas of problems of providing the qualitative health care services. This study assisted in identifying the future areas of action and recommendations for the "Manas Taalimi" strategy (2006-2010). To meet this goal a situation analysis that included description of the current content of the clinical practice in cases of AMI and strokes, their prevention, rehabilitation and the provision of drugs at the primary care and hospital care levels were carried out. The findings of this study reflected that the quality of prevention and treatment of CVD varies significantly across the regions and quite weak due to clinical and management issues.

Consequently, in 2008 based on evidence of the studies "National Programme to control CVD in the Kyrgyz Republic (2009-2013)" was developed mme (2009-2013)". The main aim of this programme to reduce CVD mortality and morbidity through a complex approach at several levels of care (population, primary health care, secondary and tertiary).

2. Objectives of study

The CVD strategy includes nearly 100 specific interventions that have evidential efficacy. However, due to financial constraints in the country, it is likely that not all interventions can be introduced at once and therefore, it is essential to prioritize the interventions to increase the effectiveness of invested funds and thereby extend coverage to more cases in need of treatment.

The goal of this analysis is to identify the set of interventions for CVD prevention and management included into the strategy that would produce the greatest health gain for available resources. In order to do this, it is important to estimate the health effects, costs and then cost-effectiveness of identified CVD interventions[8]. Here we focus on the most common causes of CVD mortality and morbidity in order to allow for more coherent and adequately directed strategy to reduce the burden of CVD: acute myocardial infarction (AMI), stroke and congestive heart failure (CHF).

The main research questions of this study are the following:

1. Which of the interventions included into this study generate the greatest health gain at the population level (as measured by disability-adjusted life years or DALYs averted)?

2. What is the relative cost of each of the interventions included into this study?

3. What is the comparative cost-effectiveness of each of the interventions (in terms of cost per DALY averted)?

4. Given the current epidemiological and economic situation, what interventions included in the strategy should be given greatest priority?

3. Methodology

3.1. The concept of cost-effectiveness analysis

Cost–effectiveness analysis (CEA) is a tool that assists policy makers to establish the priorities by evaluating outcomes (health effects) and the relative expenditure (costs) of two or more interventions. CEA is based on a ratio where the denominator is a gain in health from a

[7] Akunov N, Ibraimov A, Akkazieva B. et all. "Quality of preventive and treatment services for AMI and stroke in the Kyrgyz Republic", Policy Research Paper #45, December 2007

[8] WHO (World Health Organization). Making choices in health: WHO guide to cost-effectiveness analysis. Geneva: WHO, 2003.

measure (years of life, premature births averted, sight-years gained) and the numerator is the cost associated with achieving the health gain[9]. The results of the CEA can be interpreted as "cost" of the additional outcome purchased by switching from current practice to the new intervention (e.g., $10,000 per life year).

The interventions which provide the highest "value for money" are indicated and allow policy-makers to choose the interventions and programmes which maximize health for the available resources. By having the results of the CEA the decision-makers can improve the performance of their health systems[10].

3.2. WHO-CHOICE

There are many approaches to cost-effectiveness analysis. This study uses WHO–CHOICE method that stands for **CHO**osing **I**nterventions that are **C**ost-**E**ffective. WHO–CHOICE methodology evaluates the costs and effects of the set of interventions such as preventive, curative, rehabilitation etc. to improve health of the population[11]. The effectiveness is measured through DALYs averted – equivalent to healthy years gained - and resource cost includes costs at the patient and programme levels. Interventions are evaluated relative to an epidemiological situation of 'doing nothing' (null); the difference between doing nothing and implementing the intervention at the specified level of coverage provides the estimate of intervention impact at the level of the population [12]. The WHO-CHOICE model has been applied mainly to evaluate interventions for chronic diseases and their risk factors - such as alcohol use, blindness, depression, diabetes and CVD – as well as childhood diseases, maternal and neonatal health, schizophrenia, etc.[13]

Box 1. Definition of DALY
DALY (Disability Adjusted Life Year) is a measure of premature deaths and losses due to illnesses and disabilities in a population. It is a quantitative indicator of burden of disease that reflects the total amount of healthy life lost, to all causes, whether from premature mortality or from some degree of disability during a period of time. The DALY was first conceptualized by WHO and WB in the study known as the Global burden of disease (1996).[1].

The CVD model has been contextualized to the Kyrgyz situation by making use of the best available local data on: (a) data on local demography, including mortality rates; (b) local epidemiological rates for specified disorders; (c) intervention definition, efficacy and adherence; (d) treatment coverage and setting; (e) resource utilization rates and costs of care for specified disorders .

The following steps were undertaken to carry out the WHO CHOICE analysis:

Step 1: Identifying the interventions (section 3.3)
The set of interventions were selected for this study based on the "National Programme to control CVD in the Kyrgyz Republic (2009-2013)".

Step 2: Estimating the effectiveness of the interventions (section 3.4)
The health impact of interventions was estimated using international evidence and Kyrgyz epidemiological data. The model generated estimates of the healthy life years lived by the Kyrgyz population, both with and without interventions being in place.

[9]M.R. Gold, J.E Siegel, L.B. Russell, and M.C. Weinstein (eds). "Cost-effectiveness in Health and Medicine." New York: Oxford University Press, 1996

[11] Evans DB, Tan-Torres T., Adam T., Lim SS, the WHO-CHOICE MDG team. Achieving the millennium development goals for health: Methods to assess the costs and health effects of interventions for improving health in developing countries. BMJ 2005;331:1137-40.

[12] Hutubessy R, Chisholm D, Tan Torres T. Generalized cost-effectiveness analysis for national-level priority-setting in the health sector. Cost Effectiveness and Resource Allocation 2003;1:8.

[13] To see the full list go to http://www.who.int/choice/interventions/en/

Step 3: Estimating the cost of the interventions (section 3.5)
The cost of each intervention was estimated by applying unit costs (such as cost per inpatient day, outpatient attendance or primary care visit) to the resource utilization patterns of an average patient receiving the intervention. Costs associated with the introduction and maintenance of CVD preventive and treatment programmes are also estimated.

Step 4: Estimating the cost-effectiveness of the interventions (section 3.6)
The total costs of implementing an intervention over a period of 10 years are divided by the total health gain achieved over this same period. This gives a ratio of cost per unit of effect, which can then be compared to the cost-effectiveness ratios of other interventions in order to establish which provide the best value for money.

3.3. Identifying interventions

About hundreds Dozens of interventions are included into the "National programme to control CVD in Kyrgyz Republic (2009-2013)". From this programme we selected 29 interventions for this analysis plus a further 8 plausible combinations strategies; in total we included 37 interventions. Educational campaigns about changing the lifestyle, pharmacological and surgical interventions are included into the study and they are categorized according to the levels of care. The interventions for this study are grouped into the following categories because intervention approaches differ:

- **Primary prevention to control CVD risk factors:** (1) health education (HE) through mass media to reduce cholesterol, salt intake and smoking; (2) opportunistic screening of all people over 18 years old visiting the PHC facility for any reasons and counselling them for CVD main risk factors; (3) provision of drug treatment to lower hypertension; (4) provision of statins to lower cholesterol level to those who have over 6.2mmol/l and over 5.7mmol/l cholesterol in blood; (5) provision of combination drug therapy to those individuals who are at four (5%, 15%, 25% and 35%) levels of risk of a cardiovascular event over the next 10 years.

- **AMI acute phase (first 28 days)**: aspirin, ACE inhibitors, thrombolysis with streptokinase, primary PTCA, beta blockers and a combination of aspirin plus anti-coagulant therapy.

- **AMI post-acute phase (after 28 days):** aspirin, beta blockers, ACE inhibitors, statins, cardiac rehabilitation and secondary PTCA.

- **Stroke acute phase first (28 days)**: aspirin and organizing stroke unit care

- **Stroke post-acute phase (after 28 days):** aspirin, statins and combination of ACE-Inhibitor plus diuretic.

- **Congestive Heart Failure:** diuretics, ACE inhibitors, beta blockers and exercise training.

The list of interventions and their descriptions for the primary prevention, treatment and secondary prevention are presented in the Annex 1.

4.1. Estimating effectiveness

To estimate the population-level effectiveness or health gain of different health interventions within the framework of WHO-CHOICE we employ an epidemiological approach. Specifically, the effect of a given intervention on the health of the population is derived with reference to two epidemiological situations, one with the intervention in place, the other without the intervention (a counterfactual situation referred to as a 'null' scenario). The difference between these two situations represents the net effect of the intervention. These epidemiological scenarios are

estimated via a multi-state population model[14], which traces the development of the population taking into account births, deaths and the disease in question. This model allows to estimate health effects by tracing what would happen to each age and sex cohort of a given population over 100 years, with and without the implementation of various intervention strategies (which are implemented for only the first 10 years of this population's 100 year lifetime).

To contextualize this model to the Kyrgyz context, the best local epidemiological data on disease incidence, prevalence, remission, case fatality data etc. and demography were employed. Local and regional data on efficacy of the selected interventions, current coverage of these interventions and adherence is also required for estimation of effectiveness. To get evidences on health benefits (efficacy) of the chosen interventions we reviewed international literature that presents data from meta-analyses or at least two randomized clinical trials. The data on current coverage with these interventions, the current data on risk factors such as level of blood pressure, daily salt intake etc. and adherence were obtained from the local studies and statistics such as Kyrgyz Integrated Household Survey, "Health System Effectiveness in Hypertension Control in Kyrgyzstan"[15], "Quality of preventive and treatment services for AMI and stroke in the Kyrgyz Republic"[16]. In the Annex 2 we present two tables detailing how the data were prepared for the prevention interventions, treatment and rehabilitation interventions.

The population health level is estimated using an outcome indicator which measures changes in health taking into account fatal and non-fatal outcomes – DALYs. Hence, within the framework of WHO CHIOCE methodology the effectiveness is estimated in DALY averted by the interventions, which means measuring DALY relative to the situation of no intervention for the disease in question.

The interventions are run for 10 years and we include all benefits accruing during this period. We weighted a year of healthy life lived at young and older ages lower than a year lived at other ages (age-weighting in its base case) and without age-weighting as part of the sensitivity analysis. For this study we assumed that 80% of population in country would be covered with the interventions selected for this study.

4.2. Estimating costs

Two major types of costs were estimated, **one at the level of health facilities and patients** (e.g. inpatient days, drugs, diagnostic tests), **the other at a level above these facilities** (programme costs such as programme planning, monitoring and administration, mass media campaigns etc.). In addition, if the skills required to deliver an intervention are not available (or not yet available to the full extent necessary) in the country under study, training costs to develop those skills should be included as part of the programme costs. However if those skills are already acquired and no further training is required, the cost of the previously acquired training can be assumed to exist.

For each of the identified interventions, we estimated the resources that were required such as mass-media, diagnostic tests, drug use, medical staff, equipment etc. The prices of drugs were received from two sources: Drug Department within the MoH KR and the price list of the biggest pharmaceutical company in KR – "Neman". Unit costs of all other interventions were estimated based on experts' knowledge of market prices in Kyrgyzstan and the best available international cost information included in the WHO's costing database. We combined unit costs with patterns of resource use to estimate the cost per patient treated. Then calculating total patient costs as

[14] Lauer A., Röhrich K., Wirth H., Charette C., Gribble S., Murray Ch. "PopMod: a longitudinal population model with two interacting disease states.", Cost Effectiveness and Resource Allocation, 2003, 1:6

[15] Jakab M, Lundeen E, Akkazieva B. "Health System Effectiveness in Hypertension Control in Kyrgyzstan." Policy Research Paper #44, HPAU, CHSD, 2007

[16] Akunov N, Ibraimov A, Akkazieva B. et all. "Quality of preventive and treatment services for AMI and stroke in the Kyrgyz Republic", Policy Research Paper #45, December 2007

the cost per patient treated multiplied by the number of patients treated (calculated as the annual incidence of disease from the model multiplied by the relevant coverage level and then by the percentage of cases diagnosed and treated in the areas covered). The costs of running the programmes - that is, costs above the individual patient level, such as managerial staff - were estimated using a standardized approach. All costs are reported in Kyrgyz currency – Som for the year 2005 (see Annex 3 for a list of unit costs/price data used).

4.3. Estimating costs-effectiveness

To estimate the cost-effectiveness we have estimated effectiveness and cost separately and at the last step we run the software to establish the table with the cost-effectiveness results to see which of the interventions highly cost-effective, cost-effective and not cost-effective. The following thresholds are set up based on per capita income in Kyrgyzstan:

- 0 – 20,000 Som per DALY averted - highly cost-effective;
- 20,000- 50,000 Som per DALY averted - cost-effective;
- 50,000 Som + per DALY averted – not cost-effective.

4. Data sources

Different sources including international literature, existing WHO-CHOICE database and Kyrgyz literature were used to arrive at final data inputs (Table 1). We obtained national data for demography (age- and sex-specific population); however, for epidemiology data the results of the Global Burden of Disease (GBD) analysis (2000) was applied because such data don't exist in Kyrgyzstan yet.

Table 1. List of data and source for Kyrgyz CVD CEA

Data	Source
Demography	
Population	National Statistical Committee
Live births	Republican Medical Information Center (RMIC)
Epidemiology data	
Incidence, prevalence per 1 incidence for AMI, Stroke, Angina and CHF	WHO Regional database for the European region[17]
Ratio of first-ever AMI and stroke to all AMI By WHO Sub-Region	
24 hour Case-fatality (rate per 1 incidence) for AMI and stroke	
28-day Case-fatality (rate per 1 incidence) for AMI and stroke	
Out-of-hospital case-fatality (rate per 1 incidence) for AMI and stroke	
Mortality per 1,000 for AMI, Stroke, Angina and CHF	Republican Medical Information Center (RMIC)
% of Long Term AMI and Stroke Survivors dying from AMI and Stroke	WHO Regional database for the European region
Prevalence of CHF/prevalence for AMI survivors	
Prevalence of AP/prevalence for AMI survivors	
Risk factors	

[17] This database is based on the "Global Burden of Disease" study (1990)

Mean cholesterol level (mmol/L)	Study on defining cholesterol and salt levels (Kyrgyz-Swiss Project to support Health Reform)
SD of mean choleterol levels	
Salt intake (grams NaCl per day)	
Mean systolic blood pressure (mmHg)	Kyrgyz Integrated Household Survey, Health Module (NSC)
SD of mean systolic blood pressure	
Mean BMI (kg/mt2)	
Smoking prevalence	
SD of mean BMI	
Coverage	
% coverage of interventions for AMI and stroke during the acute phase (28-days)	Study "Quality of treatment and prevention of cardiovascular diseases in the Kyrgyz Republic" (HPAU, CHSD)
% coverage of interventions for AMI during the post-acute phase (after 28 days)	
HSV (Health State Valuations)	
Prevalent Years of Life Lost Due to Disability (pYLD) for persons without but at risk of CVD	WHO Regional database for the European region
Disability weight for AMI, Angina, CHF and stroke	
Disability weight for Long Term Stroke Survivors By WHO Sub-Region	
Efficiency	Existing efficacy in the WHO-CHOICE regional dataset, International literature review
Prices	
Prices on drugs	Department of Dugs within the MoH KG, 2008 The biggest drag store in KR "Neman", 2008
Other costs and prices relate with the programme interventions	Price list of the companies and Kyrgyz experts knowledge, Kyrgyz data 2008

5. Findings

In this section we present the cost-effectiveness of interventions and estimate the total annual cost of implementing highly cost-effective and cost-effective interventions of the strategy.

6.1. The cost-effectiveness of interventions

At the coverage of 80%, the highly cost-effective population based intervention is to educate people about reducing of smoking, cholesterol level, daily salt intake (main risk factors) via one mass-media campaign, the cost per DALY averted is 4,705 Som or US$ 129 per year per person. However, the individual mass media campaigns to reduce cholesterol level in blood and daily salt intake appeared to be highly cost-effective as well, the costs per DALY averted is 3,822 Som or US$ 105 per year per person and at the mean official exchange rate for 2008[18] and 6,304 Som or US$ 172 correspondingly.

Hypertension is a key modifiable risk-factor for cardiovascular disease and the primary care services can be effective in controlling the blood pressure of those identified as hypertensives. Our results also revealed that provision of hypertension-lowering drug treatment to an individual whose systolic blood pressure is over 160 is highly cost-effective intervention among all identified individual-based interventions at the primary care level. This intervention averts more DALYs and at lower costs per DALY – 7,615 Som or US$208. Jakab M, Lundeen E et all[19]

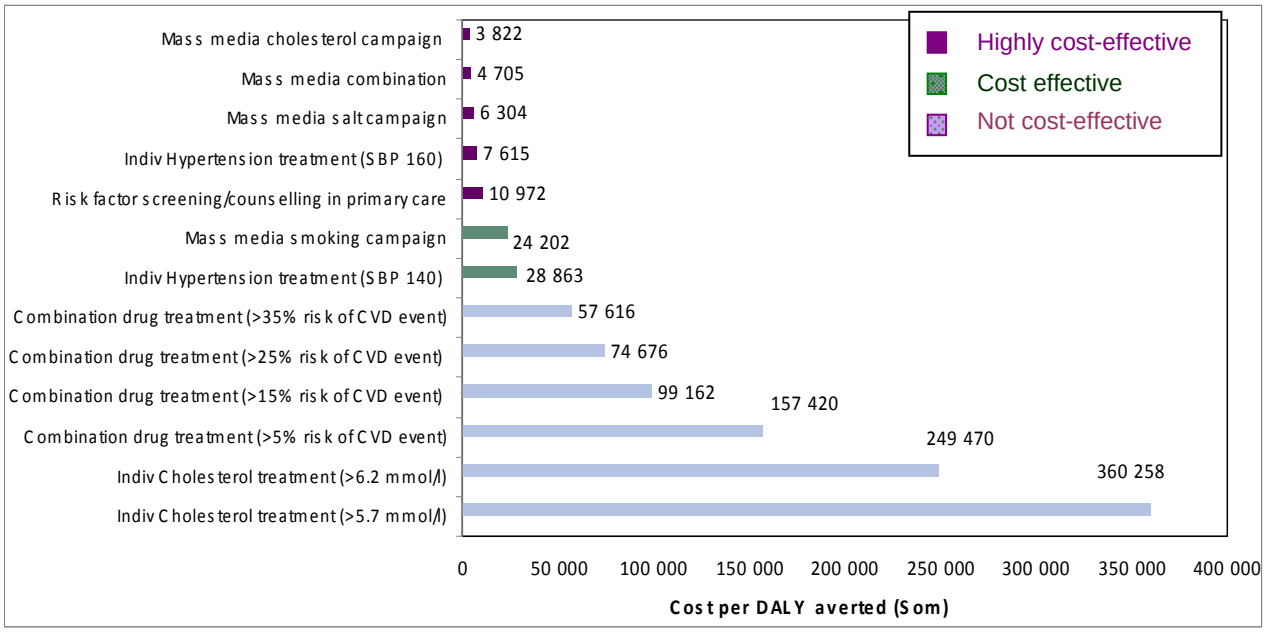
[18] *36,57 Som–1US$*

[19] Jakab M, Lundeen E, Akkazieva B. "Health System Effectiveness in Hypertension Control in Kyrgyzstan." Policy Research Paper #44, HPAU, CHSD, 2007

indicate that only 17.1% took hypertension lowering drugs in the last 24 hours among those with hypertension. Therefore it is important to follow up the patients with hypertension to take the hypertension-lowering drugs. The summary results for this level are presented in Diagram 1.

Provision of combination drug therapy to those individuals who are at four (5%, 15%, 25% and 35%) levels of risk to develop any cardio vascular disease appeared to be not cost-effective. A combination of drug therapy includes Aspirin, ACE-inhibitor and statin. One of the main reasons for this is that Statins are very expensive in Kyrgyzstan, e.g., the price of simvastatin is 37.5 Som per dose (used for this study). Providing combined drug therapy to a person at over 35% risk to develop CVD event the cost per DALY averted is less than the other three levels of risk. The other two individual-based interventions, provision of individual cholesterol treatment with Statin to those people who have over than 6.2mmol/l and over 5.7mmol/l cholesterol in blood, are not cost-effective. Again it is because of the high acquisition price of statins in Kyrgyzstanmare.

Diagram 1. Cost-effectiveness for prevention interventions at population and individual levels



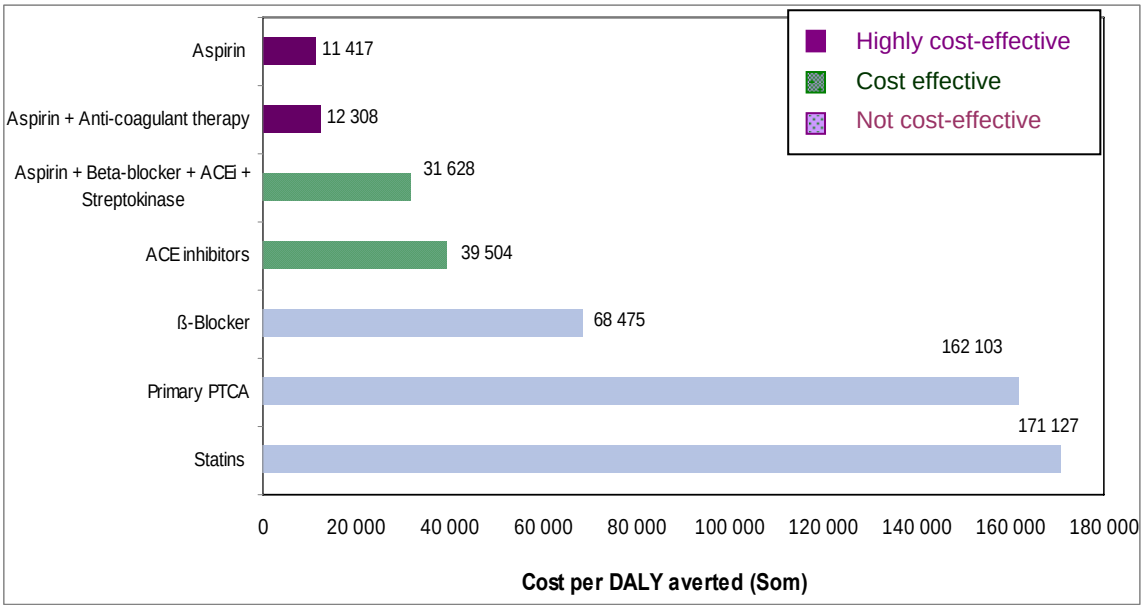
Note: with age-weighting and discounting

Aspirin is identified as the most cost-effective intervention to treat with at the acute phase of AMI with the cost per DALY averted 11,417 Som or US$312. Based on the result of the study (Akunov N, Ibraimov A, Akkazieva B., 2008) Aspirin is widely used in all regions but still not in all regions it is used[20]. According to our results combination of Aspirin and Anti-coagulant therapy could be considered also as one of the most cost-effective intervention – 12,308 Som or US$337. We looked at the international literature for the effectiveness of Anti-coagulant therapy but there is no well documented study of any additional impact over and above the use of Aspirin administered alone; however it's commonly used among doctors in Kyrgyzstan - some of them are still committed to methods that had been introduced earlier than the other methods such as Aspirin, Beta-blockers etc.[21] The combination of drugs – Aspirin, Beta blockers, ACE inhibitors and Streptokinase appeared to be quite cost-effective (31,628 Som or US$ 865 per DALY averted). Yet if only one group of drugs - ACE inhibitor – is provided at the acute phase of AMI in the hospital then it is cost-effective as well, the cost per DALY averted is 39,504 Som or US$ 1,080. The results of the intervention analysis for **acute AMI treatment** are presented in Diagram 2.

[20] A, Akkazieva B. "Quality of preventive and treatment services for AMI and stroke in the Kyrgyz Republic", Policy Research Paper #45, December 2007

[21] Akunov N, Ibraimov A, Akkazieva B. "Quality of preventive and treatment services for AMI and stroke in the Kyrgyz Republic", Policy Research Paper #45, December 2007

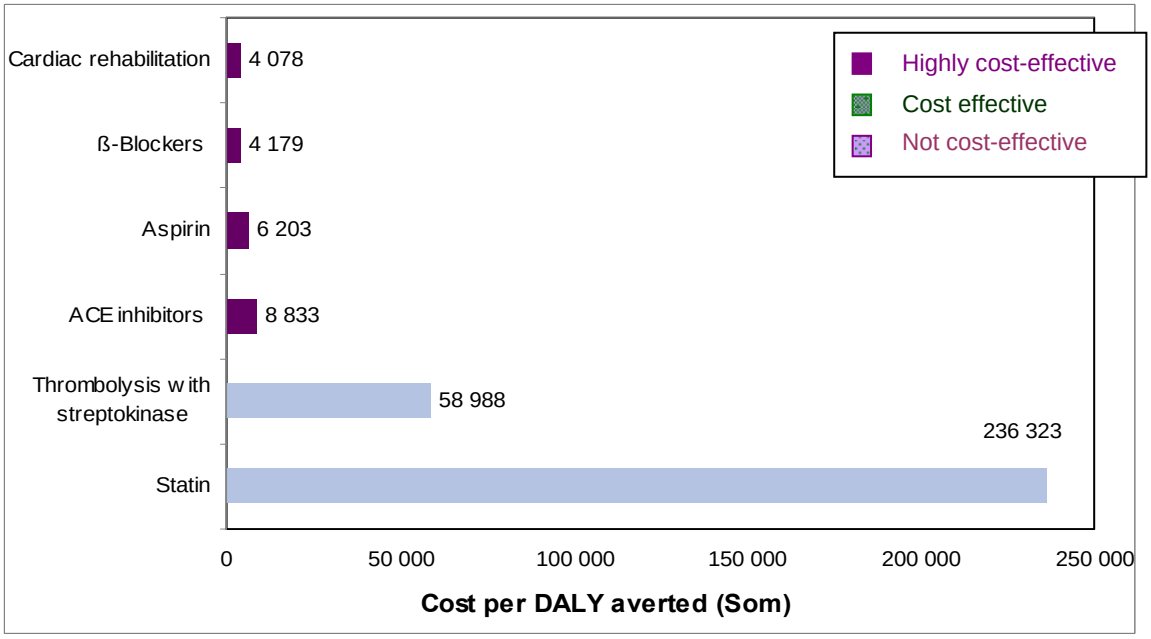
Diagram 2. Cost-effectiveness of Acute AMI treatment



Note: with age-weighting and discounting

The highly cost-effective interventions to treat post-acute AMI and provide secondary prevention are Cardiac rehabilitation, Beta blockers, Aspirin and ACE inhibitors because they avert more DALYs at lower costs per DALY – 4,078 Som or US$ 112; 4,179 Som or US$ 114; 6,203 Som or US$ 170 and 8,833 Som or US$ 242 respectively (Diagram 3). It is well known and proved internationally that cardiac rehabilitation after AMI could improve sufficiently the health status of a patient and leads to the faster recovering after this condition (IHF). The cardiac rehabilitation includes (1) exercise training and activity prescription, (2) risk factor modification (e.g. reduced tobacco use), and (3) psychosocial and vocational evaluation and counseling (for a recommended duration of at least 3 months). For Beta blockers we use atenolol at the price of 0.33 Som for a 50mg tablet. A group of drugs that are usually recommended at discharge to reduce cholesterols - Statin – was not cost-effective, the cost per DALY averted is 236,323 Som or US$ 6,462 because of high cost of statins in Kyrgyzstan. Provision of thrombolysis with streptokinase was also not found to be cost-effective, the cost per DALY averted is 58,988 Som or US$ 1,613.

Diagram 3. Cost-effectiveness of Post-acute AMI treatment and its secondary prevention

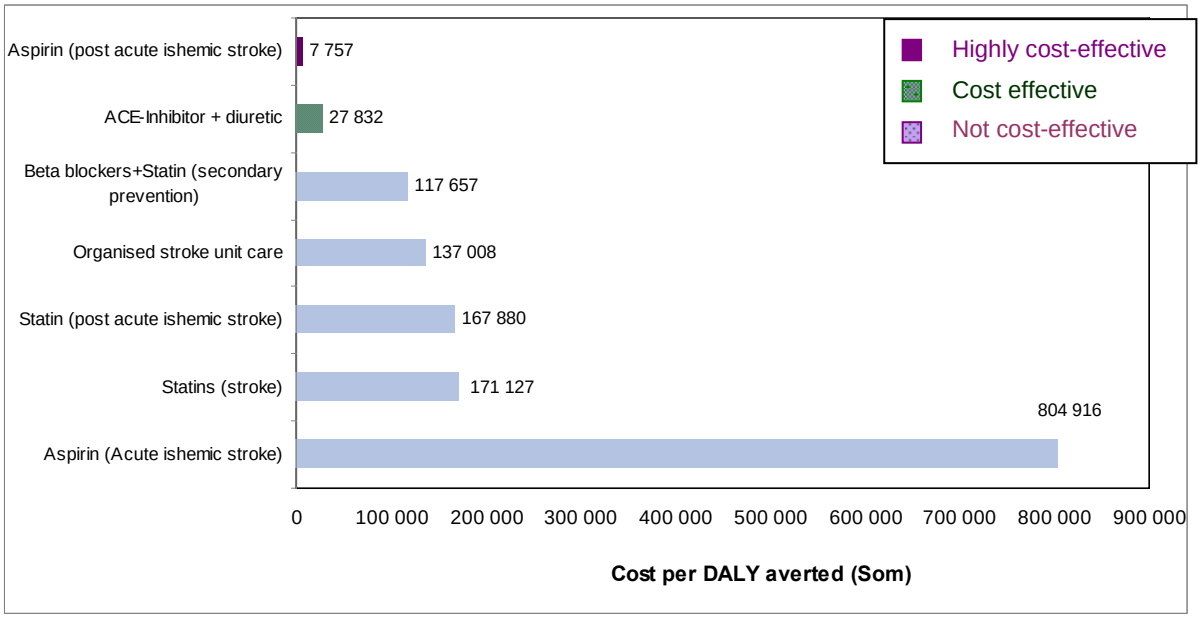


Note: with age-weighting and discounting

To treat ischemic stroke in the post acute phase with Aspirin is highly cost-effective (the cost per DALY averted is 7,757 Som or US$ 212); however the treatment of the same condition with Aspirin but in the acute phase is not cost-effective (the cost per DALY averted is 804,916 Som or US$ 22,010 per year per patient). Why is such a big difference between these two interventions? It is well known that Aspirin is an accessible drug with proven effectiveness and is considered an attested method of **treatment of ischemic stroke**. However, combination of cost and effect are differed. Based on meta-analysis of 65 trials, effectiveness for Aspirin in acute phase is 5% decrease in 30 day mortality whereas for post acute there are numerous separate effects (on AMI/CVD mortality rates as well as ischemic and hemorrhagic stroke outcomes). Regarding the cost side, because the acute phase is spent in a hospital it is quite expensive.

The other cost-effective intervention for Stroke was a combination of ACE inhibitors and Diuretics (at the discretion of treating physicians, a flexible regimen of 4mg perindopril and 25mg hyfrochlorotiazide is recommended). The summary results are presented at the Diagram 4 below.

Diagram 4. Cost-effectiveness of Stroke treatment and its secondary prevention



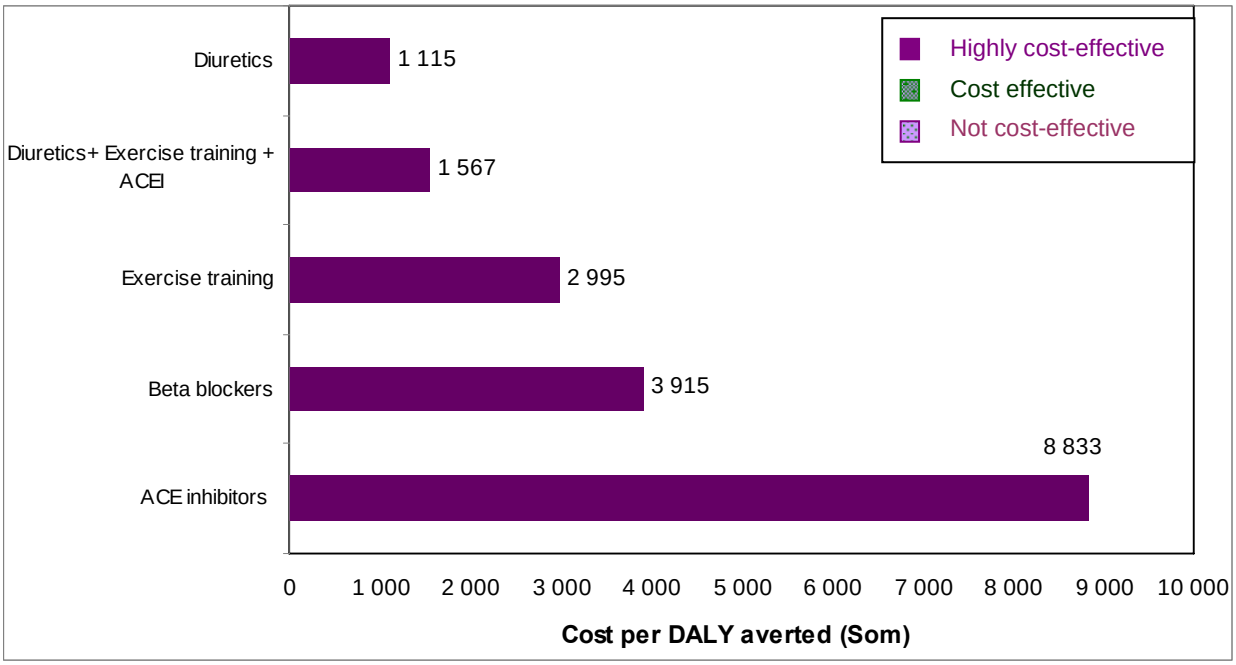
Note: with age-weighting and discounting

It is interesting that to organize stroke unit care is more cost-effective than providing patients with Statins the cost per DALY averted is 137,008 Som or US$ 3,747 and 167,880 Som or US$ 4,591 accordingly (Diagram 4). It is true that Statins are quite effective than organizing stroke unit care but this group of drugs is really expensive in Kyrgyzstan.

All five interventions to treat congestive heart failure (CHF) included in this study appeared to be highly cost-effective. Among these five interventions Diuretics is the most cost-effective; the cost per DALY averted is 1,115 Som or US$ 31. Here we used hydrochlorotiazide at the price of 4.35 Som per 25mg. The other four single and combined interventions identified for treating and secondary prevention appeared to be quite cost-effective as well, the cost per DALY averted is under 10,000 Som or US$ 273. Among these the less cost effective is ACE inhibitors, the cost of it per DALY averted is 8,833 Som or US$ 242. The summary results are presented in the Diagram 5.

In the Annex 4 we present the summary of the cost effectiveness results of all interventions that included into this study for each of CVD event.

Diagram 5. Cost-effectiveness of CHF treatment and its secondary prevention



Note: with age-weighting and discounting

6.2. Total cost of interventions

At a standardised coverage level of 80%, the total cost of separately educating the entire Kyrgyz population of 5 million people about the reduction of salt intake, cholesterol level in blood and smoking separately would be around 72 million Som per year but a combined mass media campaign about these 3 risk factors would cost only half of that cost – about 36 million Som per year (Table 2). The cost of per capita and per case within a year is the same because this intervention is spread among all population of the country.

At the primary health care level the cost of hypertension treatment of those who have SBP 160 with drugs is about around 240 million Som per year for 5,000,000 population and the cost of each case would be 1,178.10 Som.

The most cost-effective intervention for treating AMI at the hospital level – Aspirin – costs about 28 million Som per year for 5,000,000 population; for post ischemic stroke – Aspirin- about 19 million Som for 5,000,000 population, for CHF – Diuretics – about 1 million Som for 5,000,000 population. As it was highlighted the success of the treatment of any CVD even is provision of secondary preventions interventions – rehabilitation – such as exercise training and any other cardiac rehabilitation activities. The results of this study revealed that these interventions save more DALYs and are not so costly; thus, the cost of a single intervention - exercise training is about 1 million Som for 5,000,000 population and the cost of treatment of each case would be about 435 Som. To provide cardiac rehabilitation in Kyrgyzstan to each of the treated case it would cost 1,190.81 Som,

The summary results for different interventions for three CVD events (AMI, stroke and CHF) are presented in the Annex 5.

Table 2. Cost for the cost-effective interventions, Som 2008

Cost-effective interventions	Per year for 5,000,000 population	Per capita, per year	Per case, per year
Population based prevention			
Mass media cholesterol campaign	24 047 225	4,81	4,81
Mass media salt campaign	24 047 225	4,81	4,81
Mass media smoking campaign	24 047 225	4,81	4,81
TOTAL	**72 141 676**	**14.43**	**14.43**
Mass media combination	**36 466 726**	**7.29**	**7.29**
Individual based interventions			
Risk factor screening/counselling in primary care	129 492 494	25,90	518.76
Indiv Hypertension treatment (SBP 160)	240 226 075	48,05	1 178.10
Total	**369 718 569**	**73.94**	**1 696,85**
Indiv Hypertension treatment (SBP 140)	1 084 804 058	216,96	1 711,52
TOTAL	**1 454 522 626**	**290,90**	**3 408,37**
AMI			
acute phase			
Aspirin	28 163 712	5,63	3 325,09
ACE inhibitors	28 389 226	5,68	3 351,71
Total acute phase	**56 552 939**	**11,31**	**6 676,80**
post acute phase			
Beta blockers	3 337 645	0,67	110,62
Aspirin	2 318 207	0,46	76,83
ACE inhibitors	7 147 917	1,43	236,90
Total post acute phase	**12 803 768**	**3**	**424,34**
TOTAL	**69 356 707**	**14**	**7 101,15**
Stroke			
Aspirin (post acute ischemic stroke)	19 275 668	3,86	365,41
ACE-Inhibitor + diuretic (post Stroke)	127 815 241	25,56	2 423,00
TOTAL	**147 090 909**	**29,42**	**2 788,41**
CHF			
Diuretics	1 163 201	0,23	201,06
Beta blockers	1 116 043	0,22	192,91
ACE inhibitors	1 241 103	0,25	214,53
TOTAL	**3 520 346**	**0,70**	**608,50**
TOTAL TREATMENT LEVEL	**219 967 962**	**43,99**	**10 498,05**
Rehabilitaiton			
Exercise training	1 381 965	0,28	434,63
Cardiac rehabilitation	3 786 342	0,76	1 190,81
TOTAL	**5 168 306**	**1**	**1 625,44**

6. Conclusion and policy recommendations

In summary, it is essential to prioritize the interventions that have been identified in the CVD strategy while having limited financial resources. It could be done by determining the most effective and less costly interventions by applying different economics methods. For this study we applied the WHO CHOICE approach to cost-effectiveness analysis.

We found that the most **cost effective interventions** are the following in case if we provide 80% of geographical coverage with identified interventions **:**

For primary prevention to control CVD factor risks

- Mass media cholesterol campaign;
- Mass media combination: reduction of cholesterol level in the blood, daily salt intake, hypertension level and smoking;
- Mass media salt campaign;
- Individual hypertension treatment (SBP 160): interventions with drug treatment for higher risk group (SBP 160) are three times more cost effective than for lower risk group (SBP 140);
- Opportunistic screening and counseling about the main CVD risk at the primary health care level.

Acute AMI treatment

- Aspirin;
- Combination of Aspirin and Anti-coagulant therapy;
- Combination of Aspirin, Beta-blockers, ACE inhibitors and Streptokinase.

Post-acute AMI treatment and secondary prevention

- Cardiac rehabilitation;
- Beta blockers;
- Aspirin;
- ACE inhibitors.

Stroke treatment and secondary prevention

- Aspirin for the post acute ishemic stroke;
- Combination of ACE inhibitor and Diuretics;
- Beta blockers and Statin for secondary prevention.

CHF treatment and its secondary prevention

- Diuretics;
- Combination of Diuretics, Exercise training and ACE inhibitor;
- Exercise training;
- Beta blockers;
- ACE inhibitors

Based on our findings we suggest that the following interventions should be introduced at first among other identified interventions in the CVD strategy in order to control cardio-vascular disease in Kyrgyzstan:

- **Recommendation #1.** To prevent the CVD risk factors it is needed to educate population about reduction of cholesterol level in the blood and daily salt intake, control of hypertension level and reduction of smoking through a combination of mass media activities. Besides, it is needed to carry out opportunistic screening and counseling about the main CVD risk at the primary health care facilities (FMCs, FGPs,

FAPs etc.). Intervention with drug treatment for higher risk group (SBP 160) is essential.

- **Recommendation #2.** To treat AMI at the acute phase it is recommended and it is essential to provide the patients with the Aspirin at a dose of 162 to 325mg. In addition Anti-coagulant therapy could be started in the acute phase of AMI (0-36 hours). Beta-blockers, ACE inhibitors and Streptokinase could be added to the treatment regime as well. During post-acute AMI treatment it is essential to provide a patient with Beta blockers, Aspirin and ACE inhibitors.

- **Recommendation #3**. At the post acute phase the ishaemic stroke is recommended to be treated with Aspirin and in addition give a patient ACE inhibitor and Diuretics. For the secondary prevention a patient should be recommended at discharged to take Beta blockers and Statin.

- **Recommendation #4**. CHF should be treated in the hospital with Diuretics, Beta blockers and ACE inhibitor; in addition exercise training is recommended. At discharge a patient should be recommended the same pharmacological regime and exercise training.

- **Recommendation #5**. For all CVD's events a Cardiac rehabilitation is recommended. It includes (1) exercise training and activity prescription, (2) risk factors modification, and (3) psychosocial and vocational evaluation and counseling; it is proposed that the duration of it 3 months minimum.

Annexes

Annex 1. List of interventions

Table 3. Interventions for primary prevention to control CVD risk factors

	Interventions	Outcome
Population-based	Health education (HE) through mass media to reduce salt intake	Total dietary salt intake
	Health education (HE) through mass media to reduce smoking	Prevalence of smoking
	Health education (HE) through mass media to reduce cholesterol	Total blood cholesterol
	Health education (HE) through mass media to reduce hypertension	Difference between actual SBP and 115 mmHg
Individual-based	Hypertension-lowering drug treatment (DRG) and education (ED) on lifestyle modification including dietary advice	Difference between actual SBP and 115 mmHg
	Cholesterol-lowering drug treatment (statins) and education (ED) on lifestyle modification including dietary advice	Total blood cholesterol
	Combination drug therapy (Aspirin, ACE-inhibitor, statin) for at-risk patients	Absolute risk of CVD
	Opportunistic screening and counselling for CVD risk factors (smoking, BMI and SBP)	Prevalence of smoking BMI Difference between actual SBP and 115 mmHg

Table 4. Interventions for treatment and for secondary prevention, AMI, Stroke and CHF

Interventions	Description of intervention
Interventions AMI during acute phase (first 28 days)	
Aspirin (acute AMI)	Aspirin at a dose of 162 to 325 mg
ACE inhibitors (acute AMI)	Oral ACE inihibitors (captopril, enalapril, perindopril, ramipril, trandolapril, lisinopril) to patients within the first 24hrs of suspected AMI with ST elevation or with LV ejection < 40% or systolic heart failure.
Thrombolysis with streptokinase	Infusion of 1.6 million units IV over 30-60 minutes, early (0-3-12 hours after onset)
Primary PTCA	Insertion of balloon-tipped catheter into blocked area
ß-Blockers (acute AMI)	Betablockers (propranolol, metoprolol,atenolol, nadolol, timolol, acebutalol, betaxolol, bisoprolol, pindolol, labetalol*)
Aspirin (acute AMI) + Anti-coagulant therapy	Anti-coagulant drugs such as heparin, enoxapirin etc.
Interventions for AMI post-acute phase (after 28 days)	
Aspirin (post-acute IHD)	Aspirin at a dose of 75 to 150 mg
ß-Blockers (post-acute IHD)	Betablockers (propranolol, metoprolol,atenolol, nadolol, timolol, acebutalol, betaxolol, bisoprolol, pindolol, labetalol*)

ACE inhibitors (post-acute IHD)	Oral ACE inihibitors (captopril, enalapril, perindopril, ramipril, trandolapril, lisinopril) to patients post-ACS.
Statin (post-acute IHD)	HMG-CoA reductase inhibitors (pravastatin, lovastatin, simvastatin) post-ACS
Cardiac rehabilitation	Formal supervised program with the following main components (1) exercise training and activity prescription, (2) risk factor modification, and (3) psychosocial and vocational evaluation and counselling; duration for 3 months minimum
Secondary PTCA	Insertion of balloon-tipped catheter into blocked area in the post-acute phase
Interventions for Stroke during acute phase (First 28 days)	
Aspirin (acute ischemic stroke)	Aspirin at a dose of 160-300mg per day for 2-4 weeks
Organised stroke unit care	Organised system of stroke inpatient care
Interventions for Stroke post-acute phase (after 28 days)	
Aspirin (post acute ischemic stroke)	Aspirin at a dose of 75 to 150 mg
Statin (post-acute ischemic stroke)	HMG-CoA reductase inhibitors (pravastatin, lovastatin, simvastatin, cerivastatin) post-ACS
ACE-Inhibitor + diuretic (post Stroke)	Flexible regimen of an ACE-Inhibitor (4mg perindopril) with the addition of a diuretic (indapamide) at the discretion of treating physicians
Interventions for Congestive Heart Failure	
Diuretics (CHF)	Loop (furosemide) or thiazide diuretic
ACE inhibitors (CHF)	ACE inhibitor: captopril (50-100 mg TID) enalapril (10-20 mg BID) ramipril (5 mg BID) transdalopril (4 mg OD) lisinopril (30-35 mg OD) with uptitration to highest tolerance dose
Beta blockers (CHF)	Beta-blockers: cardevilol, metoprolol or bisoprolol (starting smallest does and titrating to optimal dose; e.g. 25-50 mg BID for carvedilol)
Exercise training (CHF)	Supervised exercise training

Annex 2. Effectiveness of interventions

Table 5. Effectiveness and current coverage with the preventive interventions

Intervention	Outcome	Efficacy	Source	Current Coverage
Health education (HE) through mass media to reduce salt intake	Total dietary salt intake	-15%	1-3	0%
Health education (HE) through mass media to reduce smoking	Prevalence of smoking	**-1,5%**	12-13	0%
Health education (HE) through mass media to reduce cholesterol	Total blood cholesterol	-2%	4	0%
Health education (HE) through mass media to reduce hypertension	Difference between actual SBP & 115mmHg	**-2%**	14-15	0%
Hypertension-lowering drug treatment (DRG) and education (ED) on lifestyle modification including dietary advice	Difference between actual SBP & 115mmHg	-33%	5-9	27%
Cholesterol-lowering drug treatment (statins) and education (ED) on lifestyle modification including dietary advice	Total blood cholesterol	-20%	10	5%
Combination drug therapy (Aspirin, ACE-inhibitor, statin) for at-risk patients	Absolute risk of CVD	-20%	11	70%
Opportunistic screening and counselling for CVD risk factors (smoking, BMI and SBP)	Prevalence of smoking, BMI, Difference between actual SBP and 115 mmHg	**-2%**	12-13	26%

Sources:

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Table 6. Efficacy, coverage and adherence of interventions related with treatment and rehabilitation

Intervention	Description	Notes	Comparator	Other treatments	Outcome affected	Efficacy (Mean)	Efficacy (lower limit)	Efficacy (upper limit)	References	Target Population	Current Coverage
Interventions AMI during acute phase (first 28 days)											
Aspirin (acute AMI)	Aspirin at a dose of 162 to 325 mg		Placebo		28-day mortality	-24%	SE (4%)		Meta-analysis of 65 trials (59 395 patients). ATC. BMJ 2002;324:81	Acute AMI	89%
ACE inhibitors (acute AMI)	Oral ACE inihibitors (captopril, enalapril, perindopril, ramipril, trandolapril, lisinopril) to patients within the first 24hrs of suspected AMI with ST elevation or with LV ejection < 40% or systolic heart failure.	Note: Treatment initiated in the acute phase of MI (0-36 hours) Note: Proportional benefit similar in patients at different underlying risk Note: Effect similar in those with or without Aspirin	Placebo	Streptokinase, Aspirin, beta-blockers, nitrates	28-day mortality	-7%	-11%	-2%	Meta-analysis of 4 trials (98 496 patients). ACE inhibitor Collaborative Group. Circulation 1998;97:2202-2212	Acute AMI	65%
Thrombolysis with streptokinase	Infusion of 1.6 million units IV over 30-60 minutes, early (0-3-12 hours after onset)	Greater reduction in those presenting early (0-1 35%, 2-3 25%, 4-6 19%, 7-12 16%, 13-24 5%) Meta-analysis includes SK, APSAC, tPA, UK Overlap between benefit estimate and harm benefit as half of strokes were fatal Contraindicated in those for who SK has been used previously	Placebo	Aspirin, heparin	28-day mortality	-26%			Boersma Eur Heart J 1997 18:1703-11, GISSI 334. Baigent C, Collins R, Appleby P, Parish S, Sleight P, Peto R, for the ISIS-2 (Second International Study of Infarct Survival) Collaborative Group. BMJ 1998;316:1337-43.	Acute AMI	4%
Primary PTCA	Insertion of balloon-tipped catheter into blocked area	Note: Superiority less for fibrin specific trials (RR 0.70, 0.58 - 0.85) compared to SK (RR 0.53, 0.37 - 0.75) for mortality Note: No evidence that the addition of a stent	Streptokinase		28-day mortality	-47%	-63%	-25%	Meta-analysis of 23 trials (7739 patients). Keeley et al. Lancet 2003; 361: 13-20	Acute AMI	5%
			No treatment		28-day mortality	-61%					

		provides additional mortality benefit.									
ß-Blockers (acute AMI)	Betablockers (propranolol, metoprolol,atenolol, nadolol, timolol, acebutalol, betaxolol, bisoprolol, pindolol, labetalol*)	Note: No evidence of short term benefit with acute treatment (contradicts guidelines) Note: No evidence for differentials among propranolol, timolol, metoprolol, acebutol Note: Withdrawal rate of 23.5% overall	Placebo	Pre-thrombolysis	28-day mortality	-4%	-15%	8%	Meta-analysis of 31 trials (24 974 patients). Freemantle et al. BMJ 1999;318:1730-7.	Acute AMI	75%
Aspirin (acute AMI) + Anti-coagulant therapy	Anti-coagulant drugs such as heparin, enoxapirin etc.	Commonly used in Kyrgyz Republic, but effectiveness not well established	Placebo	Thrombolysis with streptokinase	28-day mortality	-5%			One year follow-up of the ESSENCE trial (enoxaparin vs heparin in unstable angina/non-Q wave myocardial infarction):sustained clinical benefit. Goodman S, Langer A,Demers C, et al Can J Cardiol (1998) 14:122F	Acute AMI	95%
Interventions for AMI post-acute phase (after 28 days)											
Aspirin (post-acute IHD)	Aspirin at a dose of 75 to 150 mg	Note: Includes estimates for sub-optimal dose (<75mg\day) Note: No evidence of greater effect with v. high doses Note: In all high risk patients (AMI, previous stroke/TIA, previous IHD, AF, PAD, Diabetes) excluding acute stroke.	Placebo		All cause mortality	-14%	SE (2%)		Meta-analysis of 65 trials (59 395 patients). ATC. BMJ 2002;324:81	AMI (post-acute)	85%

ß-Blockers (post-acute IHD)	Betablockers (propranolol, metoprolol,atenolol, nadolol, timolol, acebutalol, betaxolol, bisoprolol, pindolol, labetalol*)	Note: No evidence of short term benefit with acute treatment (contradicts guidelines) Note: No evidence for differentials among propranolol, timolol, metoprolol, acebutol Note: Withdrawal rate of 23.5% overall	Placebo	Pre-thrombolysis	All cause mortality	-23%	-31%	-15%	Meta-analysis of 31 trials (24 974 patients). Freemantle et al. BMJ 1999;318:1730-7.	AMI (post-acute)	54%
ACE inhibitors (post-acute IHD)	Oral ACE inihibitors (captopril, enalapril, perindopril, ramipril, trandolapril, lisinopril) to patients post-ACS.	Note: Treatment initiated at varying times, 3-16 days or greater 1 month Note: Patient group heterogenous from CHD, LV systolic dysfunction, high risk (previous CHD stroke), e.t.c. Note: Effect similar in those with or without Aspirin	Placebo		All cause mortality	-18%	-25%	-11%	Meta-analysis of 6 trials (22 060 patients). Teo. Et al. Lancet 2002;360:1037-43	AMI (post-acute)	54%
Statin (post-acute IHD)	HMG-CoA reductase inhibitors (pravastatin, lovastatin, simvastatin) post-ACS	Note: Estimates confounded by non-study statin use Note: Some evidence of differential effect in secondary prevention (-24% (vs primary prevention (-27% (-35%, -19%))	Placebo	Aspirin, nitrates, ACE-inhibitor	All cause mortality	-17%	-23%	-9%	Unpublished meta-analysis of 6 trials (51 353 patients). Lim et al. 2002	AMI (post-acute)	20%
Cardiac rehabilitation	Formal supervised program with the following main components (1) exercise training and activity prescription, (2) risk factor modification, and (3) psychosocial and vocational evaluation and counselling; duration for 3 months minimum	Note: Optimal mix of components uncertain Note: Significant improvements in likelihood of precription of efficacious drugs Note: Additional improvements in risk factor profiles	Usual care		All cause mortality	-27%	-46%	-2%	Joliffe et al. Exercise-based rehabilitation for coronary heart disease	AMI (post-acute)	16%
Secondary PTCA										AMI (post-acute)	0%

Interventions for Stroke during acute phase (First 28 days)											
Aspirin (acute ischemic stroke)	Aspirin at a dose of 160-300mg per day for 2-4 weeks	Note: Treatment dependent on CT scanning 88% in CAST and 67% in IST Note: Proportion misdiagnosed as ischemic instead of hemorrhagic but no evidence of adverse effects of treatment.	Placebo		30-day mortality	-5%	SE (2%)		Meta-analysis of 65 trials (59 395 patients). ATC. BMJ 2002;324:81	Acute ischemic stroke	39%
Organised stroke unit care	Organised system of stroke inpatient care	Note: No indication that organised stroke unit care increases hospital stay	Usual care		All-cause mortality	-14%	-29%	-6%	Stroke Unit Trialists' Collaboration. Collaborative systematic review of the randomised trials of organised inpatient (stroke unit) care after stroke. BMJ. 1997 Apr 19;314(7088):1151-9.	Stroke	2%
Interventions for Stroke post-acute phase (after 28 days)											
Aspirin (post acute ischemic stroke)	Aspirin at a dose of 75 to 150 mg	Note: Includes estimates for sub-optimal dose (<75mg\day) Note: No evidence of greater effect with v. high doses Note: In all high risk patients (AMI, previous stroke/TIA, previous IHD, AF, PAD, Diabetes) excluding acute stroke.	Placebo		All cause mortality	-14%	SE (2%)		Meta-analysis of 65 trials (59 395 patients). ATC. BMJ 2002;324:81 (Figure 6)	Ischemic stroke (post-acute)	46%
Statin (post-acute ischemic stroke)	HMG-CoA reductase inhibitors (pravastatin, lovastatin, simvastatin, cerivastatin) post-ACS	Note: Estimates confounded by non-study statin use Note: Some evidence of differential effect in secondary prevention (-24% (vs primary prevention (-27% (-35%,	Placebo	Aspirin, nitrates, ACE-inhibitor	All cause mortality	-17%	-23%	-9%	Unpublished meta-analysis of 6 trials (51 353 patients). Lim et al. 2002	Ischemic stroke (post-acute)	1%

		-19%))									
ACE-Inhibitor + diuretic (post Stroke)	Flexible regimen of an ACE-Inhibitor (4mg perindopril) with the addition of a diuretic (indapamide) at the discretion of treating physicians	Note: At least 2 weeks after their most recent vascular event Note: No definite indication (such as cardiac failure) for treatment with an ACE inhibitor Note: 58% combination therapy, 42% single drug therapy	Placebo						Progress trial (combined ACEi + diuretic)	Stroke (post-acute)	37%
Interventions for Congestive Heart Failure											
Diuretics (CHF)	Loop (furosemide) or thiazide diuretic	Note: Small studies with inadequate statistical power Note: Includes loop and thiazides but not spirinolactone Note: heterogeneity in dose	Placebo		All cause mortality	-75%	-93%	-6%	Meta-analysis of 18 trials (10 placebo controlled, 10 active control; 928 patients). Faris et al. Internation Journal of Cardiology 2002;82 : 149-158.	Cardiac failure	50%
ACE inhibitors (CHF)	ACE inhibitor: captopril (50-100 mg TID); enalapril (10-20 mg BID); ramipril (5 mg BID); transdalopril (4 mg OD); lisinopril (30-35 mg OD); with uptitration to highest tolerance dose		Placebo		All cause mortality	-11%	-17%	-4%	Unpublished meta-analysis. Haas et al. 2002	Cardiac failure	43%
Beta blockers (CHF)	Beta-blockers: cardevilol, metoprolol or bisoprolol (starting smallest does and titrating to optimal	Note: Heterogeneity in treatment effect	Placebo		All cause mortality	-22%	-28%	-16%	Meta-analysis of 16 trials (14 857 patients). Bouzamondo et al. Fundamental & Clinical	Cardiac failure	23%

	dose; e.g. 25-50 mg BID for carvedilol)								Pharmacology. 2001;15: 95-109		
Exercise training (CHF)	Supervised exercise training	Note: No statistically significant subgroup specific treatment effect was observed.	Usual care		All cause mortality	-35%	-54%	-8%	Meta-analysis of 9 trials (801 patients) ExTraMATCH BMJ 2004;328;189-	Cardiac failure	12%

Annex 3. Costing of intervention

Table 7. Master Costing File tool for AMI treatment intervention with drugs at patient level

Drug	Generic names (brand names)	Route	Dose range	Daily dose	Dosage form/strenght	unit price (Som, 2007)	Cost daily dose	Cost treatment 1st year	Cost treatment 10 years	Source Drug Price	Notes	Th Initiati
ASA (primary prevention)	Aspirin	oral	100 mg/d	100 mg/d	tab/500mg	**0,046**	0,046	16,79	167,9	erc.msh.org (OECS/PPS)	Dose as per Primary Prevention Lancet paper: Murray C et al, vol 361, March 2003.	All year
Beta Blockers (primary prevention)	Atenolol	oral	50 mg/d	50 mg/d	tab/50mg	**0,33**	0,33	120,45	1204,5	erc.msh.org (CRSS)	Dose as per Primary Prevention Lancet paper: Murray C et al, vol 361, March 2003.	All year
Beta blockers (primary prevention)	**Carvedilol**	oral	25 mg/d	25 mg/d	tab/25mg	**17,8**	80,1	29236,5	292284,9	erc.msh.org (BDS)	Same dose as for secondary prevention	All year
Statin (primary prevention)	Simvastatin	oral	20 mg/d	20 mg/d	tab/10mg	**37,5**	37,5	13687,5	136875	erc.msh.org (CRSS)	Dose as per Primary Prevention Lancet paper: Murray C et al, vol 361, March 2003.	All year
Diuretic (primary prevention)	Hydrochlorotiazide	oral	25mg/d	25mg/d	tab/25mg	**4,35**	4,35	1587,75	15877,5	erc.msh.org (CRSS)	Dose as per Primary Prevention Lancet paper: Murray C et al, vol 361, March 2003.	All year
Diuretic (primary prevention)	Furosemide	oral	40mg/d	40mg/d	tab/40mg	**0,24**	0,24	87,6	876	erc.msh.org (CRSS)	Same dose as for secondary prevention	All year

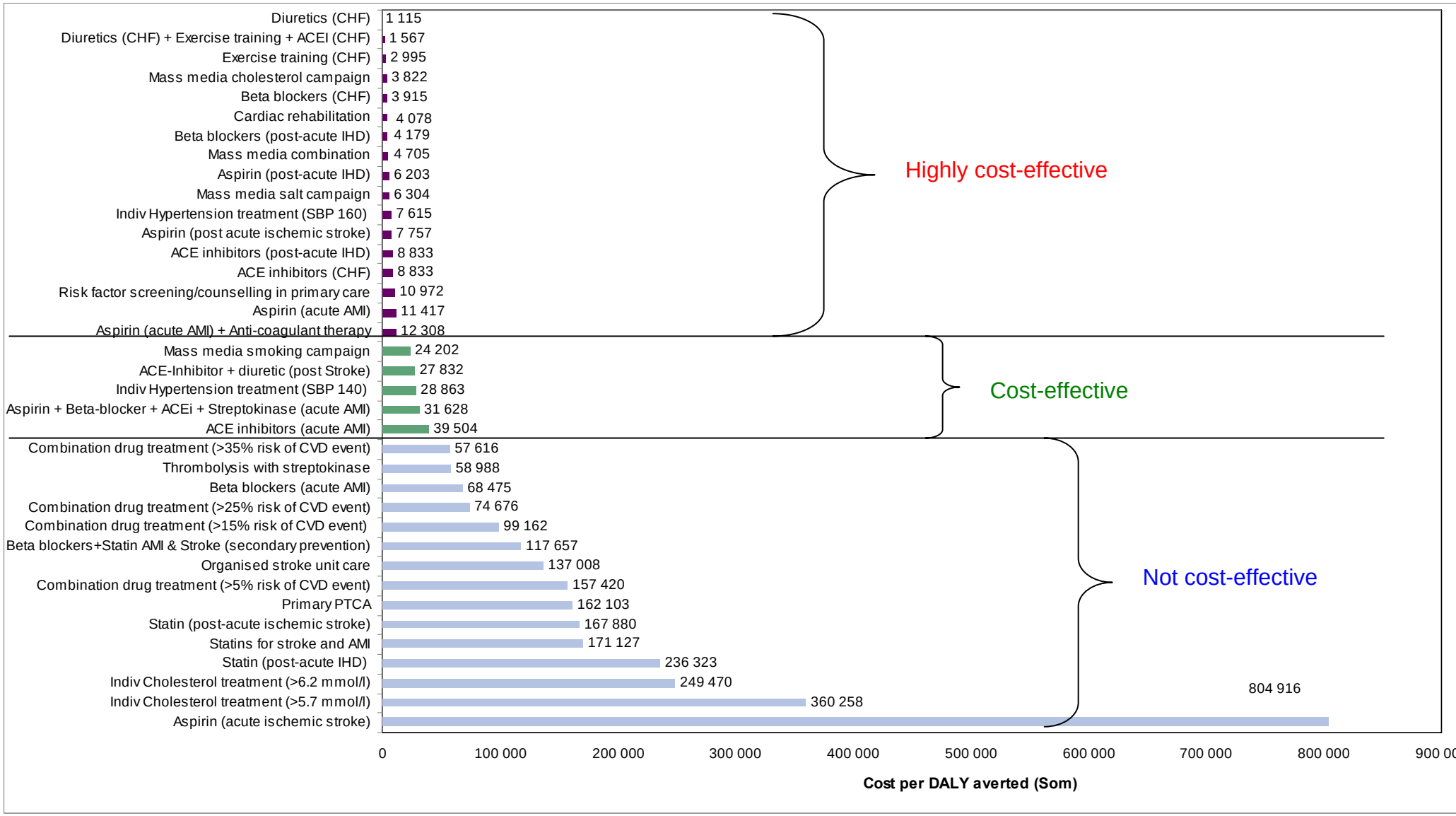
Table 8. Master Costing File tool at programme level

No.	Type of personnel (job title)	Gross salary per year
Administration		
1	Programme Director	90 000
2	Programme Manager	72 000
3	Administration Officer	48 000
4	Clerical Officer/Administrative Asst.	30 000
8	Other (Porter, Messenger, etc.)	12 000
Finance		
9	Finance Director	72 000
10	Accountant	66 000
11	Finance Officer	48 000
Health Personnel		
12	Medical Specialist	37 200
13	Medical Officer (Lowest Medical Pers)	14 400
14	Nursing Director/Manager	32 400
15	Registered Nurse	28 800
16	Health Worker	18 000
17	Director of Public Health	84 000
18	Public Health Specialist	48 000
19	Public Health Assistant	30 000
20	Health Educator/Trainer	24 000
21	Social/Welfare worker	24 000

Table 9. Media operating costs

No.	Type of media or IEC materials	Unit Cost
National Level		
1	Television time (1 minute)	7 200,00
2	Radio time (1 minute)	1 800,00
3	Newspapers (1/4 page advertisement)	12 000,00
4	Wall posters (1 sq. m.)	20,00
5	Flyers / leaflets (A4 size)	9,00
Province Level		
1	Television time (1 minute)	7 200,00
2	Radio time (1 minute)	1 800,00
3	Newspapers (1/4 page advertisement)	12 000,00
4	Wall posters (1 sq. m.)	20,00
5	Flyers / leaflets (A4 size)	9,00
District Level		
1	Television time (1 minute)	7 200,00
2	Radio time (1 minute)	1 800,00
3	Newspapers (1/4 page advertisement)	12 000,00
4	Wall posters (1 sq. m.)	20,00
5	Flyers / leaflets (A4 size)	9,00

Annex 4. Cost-effectiveness of all interventions included into the study



Annex 5. Total cost of all interventions per year for 5,000,000 population

Table 10. Cost per DALY averted per year per patient and total cost of the interventions in one year

N.	Description of intervention	Cost per DALY averted	Prevention cost per year for 5,000,000 population (Som)			Treatment cost per years for 5,000,000 pop. (Som)	Total costs per year for 5,000,000 pop. (Som)
			Patient	Programme	Training	Patient	
1	Diuretics (CHF)	1 115	-	-	-	1 163 201	1 163 201
2	Diuretics (CHF) + Exercise training + ACEI (CHF)	1 567	-	-	-	2 057 741	2 057 741
3	Exercise training (CHF)	2 995	-	-	-	1 381 965	1 381 965
4	Mass media cholesterol campaign	3 822	-	24 047 225	-	-	24 047 225
5	Beta blockers (CHF)	3 915	-	-	-	1 116 043	1 116 043
6	Cardiac rehabilitation	4 078	-	-	-	3 786 342	3 786 342
7	Beta blockers (post-acute IHD)	4 179	-	-	-	3 337 645	3 337 645
8	Mass media combination	4 705	-	36 466 726	-	-	36 466 726
9	Aspirin (post-acute IHD)	6 203	-	-	-	2 318 207	2 318 207
10	Mass media salt campaign	6 304	-	24 047 225	-	-	24 047 225
11	Indiv Hypertension treatment (SBP 160)	7 615	240 226 075	-	-	-	240 226 075
12	Aspirin (post acute ischemic stroke)	7 757	-	-	-	19 275 668	19 275 668
13	ACE inhibitors (post-acute IHD)	8 833	-	-	-	7 147 917	7 147 917
14	ACE inhibitors (CHF)	8 833	-	-	-	1 241 103	1 241 103
15	Risk factor screening/counselling in primary care	10 972	90 356 055	38 234 602	901 837	-	129 492 494
16	Aspirin (acute AMI)	11 417	-	-	-	28 163 712	28 163 712
17	Aspirin (acute AMI) + Anti-coagulant therapy	12 308	-	-	-	30 363 142	30 363 142
18	Mass media smoking campaign	24 202	-	24 047 225	-	-	24 047 225
19	ACE-Inhibitor + diuretic (post Stroke)	27 832	-	-	-	127 815 241	127 815 241
20	Indiv Hypertension treatment (SBP 140)	28 863	1 084 804 058	-	-	-	1 084 804 058
21	Aspirin + Beta-blocker + ACEi + Streptokinase (acute AMI)	31 628	-	-	-	169 073 703	169 073 703
22	ACE inhibitors (acute AMI)	39 504	-	-	-	28 389 226	28 389 226
23	Combination drug treatment (>35% risk of CVD event)	57 616	2 397 597 574	-	-	-	2 397 597 574
25	Thrombolysis with streptokinase	58 988	-	-	-	157 665 680	157 665 680

N.	Description of intervention	Cost per DALY averted	Prevention cost per year (Som)			Treatment cost per years (Som)	Total costs per year (Som)
			Patient	Programme	Training	Patient	
26	Beta blockers (acute AMI)	68 475	-	-	-	28 112 945	28 112 945
27	Combination drug treatment (>25% risk of CVD event)	74 676	3 474 761 148	-	-	-	3 474 761 148
28	Combination drug treatment (>15% risk of CVD event)	99 162	5 150 140 034	-	-	-	5 150 140 034
29	Beta blockers+Statin AMI & Stroke (secondary prevention)	117 657	-	-	-	833 004 348	833 004 348
30	Organised stroke unit care	137 008	-	-	-	110 751 061	110 751 061
31	Combination drug treatment (>5% risk of CVD event)	157 420	9 369 607 839	-	-	-	9 369 607 839
32	Primary PTCA	162 103	-	-	-	1 015 390 065	1 015 390 065
33	Statin (post-acute ischemic stroke)	167 880	-	-	-	709 231 522	709 231 522
34	Statins for stroke and AMI	171 127	-	-	-	812 262 686	812 262 686
35	Statin (post-acute IHD)	236 323	-	-	-	123 059 909	123 059 909
36	Indiv Cholesterol treatment (>6.2 mmol/l)	249 470	3 417 150 074	-	-	-	3 417 150 074
37	Indiv Cholesterol treatment (>5.7 mmol/l)	360 258	6 613 090 803	-	-	-	6 613 090 803
38	Aspirin (acute ischemic stroke)	804 916	-	-	-	120 226 636	120 226 636

Note: The interventions highlighted in red are highly cost-effective;

The interventions highlighted in green are cost effective;

The interventions highlighted in blue are not cost-effective.