Den Sooluk

HEALTH POLICY ANALYSIS CENTER

Policy Research Paper

Cost estimation of medicinal treatment of hypertension in the Kyrgyz Republic with the view of creating possible drug supply mechanisms ensuring free-of-charge HTN treatment

Bishkek - 2014

World Health Organization
REGIONAL OFFICE FOR Europe

Schweizerische Eidgenossenschaft
Confédération suisse
Confederazione Svizzera
Confederaziun svizra

ABSTRACT

Hypertension is an important factor of mortality and disability from cardio-vascular diseases in the Kyrgyz Republic. Hypertension in combination with hyperlipemia and coronary heart disease in 80 % of cases is the cause of mortality and disability resulting from cardio-vascular diseases. According to the research lately carried out the prevalence of hypertension increases amounting to 34% of individuals over 18 years old. The research is mainly focused on estimation of financial expenses on purchase of pharmaceuticals for treatment of hypertension in the Kyrgyz Republic. Calculation data may be the basis to consider mechanisms of providing subsidized pharmaceuticals for patients with hypertension as the incentive to improve diagnostics and continuous control of hypertension.

Authors: Abdraimova A. (HPAC), Urmanbetova A.(HPAC), Borchubaeva G. (MHIF), Azizbekova J. (MHIF)

Requests about publications of the Public Fund "Health Policy Analysis Center" should be addressed to:

PF "Health Policy Analysis Center"
Kyrgyz Republic
Bishkek 720040
Togolok Moldo Str., 1 (offices ##201,203,205)

Or by e-mail: office@hpac.kg

In addition, information about the Center and prepared policy research papers as well as policy briefs and other documents may be found on the website of the Health Policy Analysis Center www.hpac.kg

This report was prepared with technical support of the WHO Regional Office for Europe through the biennial collaborative agreements (BCA) covering 2012–2015, between the Ministry of Health Kyrgyzstan and the World Health Organization (WHO). It was produced with the financial assistance from the SDC (The Swiss Agency for Development and Cooperation) to WHO for the project "Strengthening Monitoring and Evaluation and Policy Dialogue for Den Sooluk". The selection and interpretation of the conclusions reflected in this report belong to the team that drafted the report and do not necessarily reflect the official opinions of SDC and WHO.

TABLE OF CONTENTS

LIST OF ABBREVIATIONS

ABP	Arterial Blood Pressure
ADP	Mandatory Health Insurance Additional Drug Package
AH	Arterial Hypertension
CIHS	Comprehensive Integrated Household Survey
CVC	Cardio-Vascular Complications
CVD	Cardio-Vascular Diseases
HTN	Hypertension
HPAC	Health Policy Analysis Center
HVHR	High and Very High Risk
INN	International Nonproprietary Name (for pharmaceutical substances)
KR	Kyrgyz Republic
MHIF	Mandatory Health Insurance Fund under the Government of the KR
MOH	Ministry of Health of the KR
MR	Moderate Risk
NCCT	National Center for Cardiology and Therapy
SGBP	State-Guaranteed Benefit Package

ACKNOWLEDGEMENTS

Health Policy Analysis Center extends its deep gratitude for the support provided by the Ministry of Health of the Kyrgyz Republic to this study which has been carried out in the framework of the National Den Sooluk Health Care Reform Program (2012-2016).

The HPAC team is particularly grateful to Dr. Barton Smith, Deputy Regional Director of the USAID-funded “Health Quality” Project, Dr. Kadyralieva R.B., Deputy Director of the National Cardiology and Therapy Center, Ms Borchubaeva G.Sh., Head of Finance and Economics Department in the MHIF, Ms Azizbekova Dz.A., Head of the Department for MHI programs implementation in the MHIF, for their advice, feedback and contributions to the research design and this paper preparation.

The preliminary results have been communicated and discussed at the Joint Annual Review of the National Den Sooluk Health Care Reform Program (2012-2016) in November 2014. Final report has been prepared considering the obtained feedback and recommendations.

1. RESEARCH BACKGROUND

Hypertensive disease is the leading cause of mortality and disability in Kyrgyzstan among other cardio-vascular diseases (CVDs). It was demonstrated that share of hypertensive disease combined with hyperlipidemia and coronary heart disease that contribute to mortality and disability rates from CVDs measures up to 80%[1]. Hypertensions incidence continues to grow reaching from 30.1% in adult population (according to standardized 2007 CIHS findings) to 34.1% in the age group of 18+ (according to 2012-2013 Interepid survey findings).

CVD control has been identified as one of the priorities in all Kyrgyz health reform programs (Manas, Manas Taalimi, Den Sooluk for 2012 – 2016). Den Sooluk program segregates measures on improvement of hypertensive disease detection and control into separate group of performance indicators on CVD which in combination with other performance indicators are expected to lead to annual 1% reduction in CVD mortality rates.

Kyrgyzstan has made tremendous efforts to improve primary health care. Hypertension control was emphasized in this process as one of the monitored conditions.

In addition, State-guaranteed Benefit Package (SGBP) and Additional Drug Package for insured population at outpatient level were designed to ensure affordability of health services on detection and treatment of various conditions including hypertension.

The focus of this research was to study the issue of affordability of antihypertensive drugs, i.e. cost of drug therapy, **since effective hypertension control can improve health outcomes by reducing acute CVD cases such as stroke and myocardial infarction and be cost-effective for the health system** by reducing hospitalization rates. This was also driven by the results of several studies and the trend of drug supply and consumption in the country.

First, the "Health system effectiveness in hypertensive disease control in Kyrgyzstan"[2] study implemented by WHO in 2007 suggests that only **57% of those who were aware of having hypertension administered antihypertensive drugs in the recent 24 hours**. Of those who didn't take drugs in the recent 24 hours despite the available prescription **10% of respondents reported financial barrier to be the reason for not procuring the drug**. The authors make an assumption that this figure could be higher than 10% if the question asked about receiving treatment in general rather than taking drug in the recent 24 hours. Unfortunately this subject was not additionally explored and the assumptions of authors are not supported by direct prove.

Second, the amount of out-of-pocket expenditures for health services has increased 3.5 times in the recent decade – from 1.5 billion KGS in 2000 to 5.6 billion KGS in 2009. **Expenditures on drugs constitute up to 60% within the structure of out-of-pocket expenditures**. Household expenditures on drugs adjusted for inflation have increased almost twofold[3] in the period of 2000 – 2009. Expenditure pattern of people aged 50 and above shows that 1/3 of their income belongs to drug expenditures. Such pattern may have a significant effect on continuous use of

[1] Djumagulova A. S., Mirrahimov E. M. Primary and Secondary Prevention of Arterial Hypertension and Hypercholesteremia in the Kyrgyz Republic. Central-Asian Medical Journal 1997; 1: 35-39
[2] This survey used representative sample of households with standardized questionnaire results.
[3] HPAC: CIHS, NHA – 2009

drugs for chronic disease management including hypertension especially for low-income population groups[4].

Third, the analysis of MHI ADP shows that up to **70% of antihypertensive drugs prescribed by the doctor under the ADP had brand names[5] which, as a rule, are more expensive than generic drugs with International Nonproprietary Name (INN)**. This affects the financial burden of the patients and forces down their adherence to uninterrupted drug intake.

In the context of the above mentioned problems and the emphasis made by Den Sooluk program on elimination of barriers to services current research sets an objective to estimate cost of medicinal treatment of hypertension based on approved clinical guidelines of HTN treatment in adults. Estimations can be used as grounds for consideration of mechanisms ensuring free provision of antihypertensive drugs to incentivize improved HTN diagnostics and uninterrupted control.

2. RESEARCH GOAL AND OBJECTIVES

Goal of this research is to estimate cost of treatment of hypertension (HTN) as consistent with clinical guideline for HTN treatment with due consideration of incidence rate and risk of cardio-vascular complications.

Main research questions:

1. To what extent do existing drug benefit programs cover HTN patients with drugs?
2. Cost analysis of main drugs used for HTN treatment in Kyrgyzstan.
3. What is the cost of medicinal treatment of HTN as consistent with clinical guideline for HD treatment with due consideration of incidence rate for different categories of patients (including the risk of elevated blood pressure, cardio-vascular complications and co-morbidities)?

3. METHODOLOGY

3.1 Analysis of drug benefit programs coverage of HTN patients

During the discussion of issues related to cost estimation of medicinal treatment of HTN and possibility of free drug provision with the stakeholders some of them expressed the opinion that the existing program at outpatient level (MHI ADP) was sufficient and that there was no need in additional provision of subsidized drugs to HTN patients. To verify this opinion it was decided to analyze the pattern of drug use by HTN patients and the coverage of HTN patients with indicated program. The analysis was reposed on data from MHIF database.

3.2 Cost analysis of main drugs used for HTN treatment

To date, the country has a large market for drugs to treat hypertensive disease and prices vary across the range. Two types of expenses for HTN treatment were used to estimate the cost of medicinal treatment – using the price of the cheapest generics with INN available in the market

[4] HPAC: National Drug Policy Analysis, 2007-2010
[5] HPAC: Health system effectiveness in hypertensive disease control in Kyrgyzstan, 2007

and generic drugs with brand names which were manufactured in European countries with strict regulations and have GMP compliance certificate.

The reason for which estimation of cost of treatment was done with use of INN generics and generics with brand names having guaranteed quality is attributed to inadequate control of therapeutic efficacy of drugs and high probability of presence of generics with low clinical efficacy in the market nowadays.

The 2008 study on quality of drugs in pharmaceutical sector[6] which included assessment of about 10% of registered for the time being drugs used for treatment of the most prevalent conditions including hypertension suggested that there were drugs with low clinical efficacy offered in the market. Findings of this study showed that only 30% of drugs came from manufactures that passed WHO audit for GMP standards compliance or were imported from countries with strict regulators. At the same time this study showed that high price for drug is not always a measure of good quality.

Taking into account the fact that Kyrgyzstan has a widespread practice of prescribing advertised brand analogues of drugs this issue gains critical importance in hypertensive disease treatment since inefficient drugs may lead to acute conditions in patients while continuous treatment with more expensive brand analogues may have a drastic effect on financial burden and adherence to uninterrupted intake of medicines. The situation is complicated by the fact that neither the patient nor the doctor can objectively assess the efficacy and quality of drugs available in the market.

3.3. Cost estimation of medicinal treatment of hypertension

Basic approach used for cost estimation of medicinal treatment of hypertension among the Kyrgyz population.

Considering incidence of hypertension in January 2013, the number of officially registered patients with HTN was 4.1% of adult HTN patients (above 18). However, the most recent studies on arterial hypertension incidence give evidence of insufficient level of registration and limited data on hypertension incidence. Findings of 2007 CIHS suggest that HTN incidence was 28.4% in Kyrgyzstan. When these results are standardized against the world population for the purpose of international comparison this figure raises to 30.98%. Moreover, according to 2012-2013 Interepid survey findings HTN incidence was 34.1% of the adult population (above 18) of the country.

Discrepancies between the official figures and the two mentioned survey findings indicate drawbacks in the system of HTN detection, registration and treatment. Nonetheless, expected outcomes of Den Sooluk program presume increased number of detected HTN cases at the primary care level by 10% annually with baseline incidence rate of 4.1% of adult population. Thus, the target for improved coverage of HTN patients with treatment was set by Den Sooluk at 6.1% of adult population for the year 2016.

[6] Quality of drugs in the public procurement sector in the KR, WHO. 2008

Due to the above-mentioned indicators, cost of HTN treatment was estimated using three scenarios – i) coverage of registered HTN patients (4.1% of adult population); ii) target coverage of HTN patients (6.1% of adult population); and iii) HTN incidence as per Interepid data – 34.1% of adult population.

- Stratification of HTN patients by additional risk of cardio-vascular complications to define HTN treatment schemes with drugs.

According to 1999 WHO/ISH recommendations "major objective of antihypertensive treatment is to ensure maximum risk reduction of cardio-vascular incidence and mortality in HTN patients". This means that when providing treatment to HTN patients it is required to not only lower the blood pressure to optimal value but also address other risk factors resulting in cardio-vascular complications (CVC). Moreover, presence of risk factors determines the scheme of HTN patient treatment.

At present, Kyrgyzstan is experiencing significant changes with regard to managing patients with hypertension due to endorsement of National clinical guideline for HTN treatment in adult population.

Approved clinical guideline for HTN treatment determines treatment schemes of HTN patients on the basis of rise in blood pressure as well as presence or absence of associated risk factors (RF), subclinical target lesions (TL) and associated clinical conditions (ACC). Same level of blood pressure can be considered unacceptably high for high-risk patient and acceptable for low-risk patient.

Therefore, when defining medicinal treatment schemes we based our judgment on risk assessment of cardio-vascular complications as the major indication for medicinal intervention and on blood pressure level as complimentary indication for prescription of medicine. In other words, standard treatment scheme assumes that selected medicine should not only lower the blood pressure but also improve (or at least not aggravate) the course of associated conditions and have the highest possible efficacy and evidence base.

To capture data on HTN patient stratification by risk of cardio-vascular complications we used data from international guidelines for the management of arterial hypertension[7], clinical research on stratification of patients by additional risk of cardio-vascular complications[8] and also data from local studies.[9,10]

Since medicinal therapy for patients with low risk of cardio-vascular complications depends to a greater extent on effectiveness of non-medicinal therapy and most commonly does not require administration of medicines[11] no estimations of medicinal treatment of HTN with low risk of cardio-vascular complications were undertaken.

[7] Guidelines for the Management of Arterial Hypertension (ESC, 2007)
[8] Cardiovascular risk in patients with arterial hypertension: an evolution of views, The Russian University of National Friendship, «Moscow, Russia»
[9] CIHS, 2011
[10] Interepid NCCT, 2013
[11] European Society of Hypertension–European Society of Cardiology guidelines for the management of arterial hypertension. Guidelines Committee. Journal of Hypertension 2003, www.eshonline.org

- Use of optimal combination of long-acting drugs with consideration of blood pressure elevation degree and CVC risk

Cost estimation of medicinal treatment of HTN entailed usage of optimal combination of long-acting drugs with the aim of achieving ultimate hypotensive action and minimizing adverse effects on the basis of approved clinical guideline for HTN treatment in adult population (2010).

4. FINDINGS

4.1. Analysis of HTN patients coverage with drug benefit programs

It is obvious nowadays that there is need to **further develop and strengthen the role of national drug benefit programs** at the outpatient level. MHI Additional Drug Package was designed to reduce burden of drug expenses on the people including HTN patients through partial reimbursement of drug cost, ensure adherence to proper prescription practices and reduce hospitalization rate for those conditions that can be effectively managed at the primary care level. However, practical implementation of such programs faces obstacles that hinder their effective implementation. Hence, it is necessary to: 1) revise mechanisms of drug benefit program implementation to improve targeting; 2) increase funding level of drug benefit programs; 3) influence drug prices in return for guaranteed volume of sales; 4) influence providers of health services to choose between INN generics and generics with brand names.

Currently ADP as part of service delivery includes 15 drugs for treatment of hypertension which makes 17% of the total list of reimbursed drugs. Capitation rate allocated for ADP is less than 1 USD per 1 person per year. With limited available funds all insured citizens have equal entitlement under this program and no other criteria – such as social status or chronic condition – are taken into consideration. The only prerequisite for prescription of drug at a reduced price is medical indications.

Thus, in 2013, ADP has issued 285 thousand prescriptions to 120.9 thousand HTN patients for the amount of 45.9 million KGS which makes up 26% of total budget allocated for ADP. Actual reimbursement amount for sold drugs in 2013 was 185.8 million KGS.

It turns out that one HTN patient gets no more than 2 prescriptions per year on average. One prescription prescribes course dose for no longer than 1 month. In other words, HTN patients who receive drugs under this program are provided with necessary drugs only for 2 months a year at max. Mindful that HTN patients must take drugs continuously, one can say that provision of such limited amount of drugs under the benefit program cannot ensure effective control of hypertension.

Besides, implementation of such programs also indicates insufficient use of cheaper generic drugs. Analysis of MHIF data suggests that only 30% of funds allocated for patient reimbursement through MHI ADP are spent to reimburse drugs with generic names while 70% of funds are spend for more expensive generics with brand names.

4.2. Price analysis of main drugs used for HTN treatment

Estimation of HTN treatment cost was done through calculation of optimum combinations of 5 drugs of which 3 drugs are the first-line drugs for HTN treatment pursuant to the approved

clinical guideline: diuretics – Hydrochlorothiazide, calcium antagonists – Amlodipine and ACE inhibitors – Lisinopril. Treatment scheme for patients with high and extremely high risk of cardio-vascular complications also includes hypolipidemic agent – Atorvastatin and antiaggregant – Acetylsalicylic acid.

All indicated drugs are included in the Essential Drug List and authorized for use in the country.

As per the Register of drugs authorized for use in Kyrgyzstan the following drugs are available in the market – 19 brand names of Amplodipine, 3 names of Hydrochlorothiazide, 16 brand names of Lisinopril, 13 names of Acetylsalicylic acid and 9 generic names of Atorvastatin.

We selected the cheapest generic drugs with INN and generic drugs with brand names which have GMP compliance certificate audited by WHO or were imported from European countries with strict regulations.

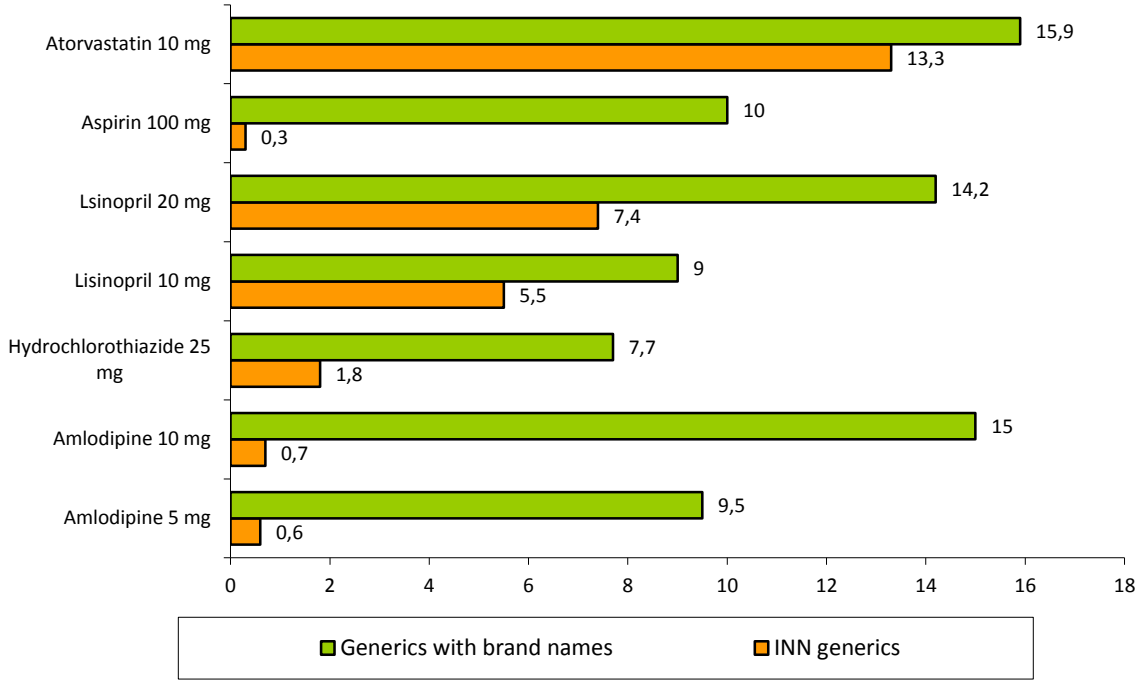
Drug prices were obtained from the DDPME database of wholesale prices for drugs as of September 2013.

Drugs selected for estimation have a wide range of prices. Substantial price difference was observed for Amlodipine with very high price variation (up to 15 times). It should be mentioned that the price of selected generics with brand names are not the highest of all the drugs available in the market.

The most expensive drugs belong to the group of statins – atorvastatines. It should be noted that in this group of drugs there is no big difference in price for generics with INN and generics with brand names (Picture 1). Despite the fact that 9 generic names of Atorvastatin are registered in the market all these drugs were available primarily in the pharmacy chain of the capital city. Data on imported quantities of Atorvastatin make it obvious that this drug is not consumed in large quantities in Kyrgyzstan and, hence, low competition does not facilitate cut in prices. This can be attributed to therapeutic practices of the doctors' not prescribing statins on a regular basis regardless of the fact that they are described in clinical guidelines as required drugs for patients with high risk of CVC.

In 2013, the country imported only 5 types of generic Atorvastatins out of 9 authorized generics with the total number of tablets equaling to 1.187 million. Assuming that patients take this drug daily in minimal dose – 1 tablet (10 mg), the above-mentioned quantity may suggest that only about 3252 patients in the whole country consume this drug on a regular basis. Estimation below suggest that the number of registered II and III degree HTN patients with high and extremely high CVC risk for which it is recommended to consume statins amounts to 52 thousand.

Picture 1. Prices for selected drugs (per 1 tablet/KGS)



Source: DDPME database of wholesale prices for drugs

4.3. Cost estimation of medicinal treatment of hypertension

- **HTN incidence structure by degrees**

Cost estimation of HTN treatment with account of incidence rate entailed use of findings from NCCT and Interepid studies. According to these findings, hypertension incidence rate is 34.1% in adult population (with 3 596 360 adults in 2013), i.e., 1 226 346 people.

Clinical guideline for HTN treatment in adults approved in Kyrgyzstan follows classifications proposed by WHO (1999), European Society of Cardiologists (ESC/ESAH, 2007) and RSSC (2009) and defines three degrees of blood pressure elevation.

I degree HTN	**140-159**	**90-99**
II degree HTN	**160-179**	**100-109**
III degree HTN	**≥180**	**≥110**

Within the scope of Interepid study the following data on blood pressure were obtained and grouped by degrees according to the approved classification: 61% of patients have I degree HD, 23% - II degree HD and 16% - III degree HD (see the table below):

HTN	In %	In absolute figures
I degree	**61 %,**	**748 035**
II degree	**23%**	**280 513**
III degree	**16%**	**197 798**
Total:		**1 226 346**

- **Stratification of HTN patients by complementary risk of cardio-vascular complications**

Data from international clinical guidelines for HTN treatment and findings from studies on stratification of HTN patients by CVC risk were used to stratify HTN patients in Kyrgyzstan by risk of cardio-vascular complications. According to utilized data, about 6% of patients with I degree elevation of blood pressure typically have moderate risk of CVC, 94% have high and extremely high CVC risk. Among II degree HTN patients 17% have moderate CVC risk and 83% have high and extremely high risk of CVC. All patients with III degree HTN have high and extremely high risk of cardio-vascular complications. They are subject to combined antihypertensive therapy intensified by statin and antiaggregant. Patients with low risk of CVC constitute less than 1% and do not need medicinal therapy provided that they follow basic measures on life style modification.

This composition of HTN patients by degrees and risks was utilized for estimation of HTN patients by CVC risks in the KR.

Two-step approach was used for estimation of HTN incidence by CVC risk applying the above-mentioned structure:

1. Extrapolation of incidence structure by CVC risk to incidence structure by HTN degrees from the Interepid study.
2. Obtained absolute figures were used for development of HTN incidence structure by CVC risk.

Extrapolation of incidence structure by CVC risk to incidence structure by HTN degrees from the Interepid study (34.1% or 1 226 346 people) resulted in the following figures:

Table 1. Extrapolation of HTN incidence structure by CVC risk

	Number of HTN patients by degrees (Interepid, 2013)	**Estimated number of HTN patients with moderate CVC risk**	**Estimated number of HTN patients with high and extremely high CVC risk**
I degree HTN	748 035	44 882 (6%)	703 153 (94%)
II degree HTN	280 513	47 687 (17%)	232 826 (83%)
III degree HTN	197 798		197 798 (100%)
Total:	**1 226 346**	**92 569**	**1 133 777**

Therefore, all 197 798 patients with III degree HTN as well as the majority of HTN patients with I and II degrees were assigned to the group high and extremely high CVC risk.

Then estimated number of patients with the breakdown by degrees and risk were used to compile HTN incidence structure as percent of total number of HTN patients obtained from Interepid findings (34.1% of adult population in the KR) (Table 2).

Table 2. Estimated number of HTN patients, in %, by risk and blood pressure degree

	% of HTN patients with moderate CVC risk	% of HTN patients with high and extremely high CVC risk
I degree HTN	44 882 (3.66%)	703 153 (57,34%)
II degree HTN	47 687 (3.88%)	232 826 (19%)
III degree HTN		197 798 (16.1%)
Total:		**1 226 346 people (100%)**

These estimations suggest that in Kyrgyzstan patients with high and extremely high CVC risk constitute up to 93% of all HTN patients identified by the Interepid study. The most prevalent group consists of patients with I degree HTN and high and extremely high CVC risk (57.3%). Obtained findings will be used for cost estimation of drugs required to provide proper treatment to HTN patients depending on CVC risk on condition of 100% patient coverage.

This structure of HTN incidence by CVC risk was used to estimate the number of HTN patients with 6.1% coverage of adult population (219 989 people) which is the target indicator from Den Sooluk program and with 4.1% coverage of HTN patients (147 429 people) which is the baseline indicator from Den Sooluk program reflecting registered number of HTN patients.

Table 3. Estimated number of HTN patients by degrees and CVC risk with 4.1% coverage of adult population

	Number of HTN patients moderate CVC risk	Number of HTN patients with high and extremely high CVC risk
I degree HTN	5 396 (3.66%)	84 544 (57,34%)
II degree HTN	5 734 (3.88%)	28 016 (19%)
III degree HTN		23 739 (16.1%)
Total:		**147 429 people (100%)**

Table 4. Estimated number of HTN patients by degrees and CVC risk with 6.1% of adult population

	Number of HTN patients moderate CVC risk	Number of HTN patients with high and extremely high CVC risk
I degree HTN	8 052 (3.66%)	126 154 (57,34%)
II degree HTN	8 556 (3.88%)	41 804 (19%)
III degree HTN		35 423 (16.1%)
Total:		**219 989 people (100%)**

- **Define medicinal treatment scheme of HTN taking into account the risk of cardio-vascular complications and blood pressure elevation degree**

According to the clinical protocol approved in the KR, composition of medicinal therapy for HTN treatment depends on: 1) cardio-vascular complications risk assessment; 2) degree of arterial hypertension; and 3) presence of associated conditions. Application of these medicinal schemes is intended to gain ultimate hypotensive action and minimize adverse effects in adult population.

Therapy schemes from the KR protocol are not standard therapy schemes applied as treatment regimen to treat, for example, some infection diseases. Treatment of hypertension entails individual approach to each patient. Application of standard schemes of medicinal treatment could improve reliability of cost estimation of treatment. Therapy schemes provided in the protocol with regard to HTN are optimal depending on the extent of accumulated CVC risk and blood pressure level. In the schemes of medicinal treatment and cost estimations provided below we made assumptions that doctors closely confine to these schemes when prescribing treatment to HTN patients with different degrees of blood pressure elevations and CVC risk.

Recommendations from the approved protocol for HTN treatment and opinions of surveyed experts fed compilation of matrix of drug combinations which form the basis of these therapy schemes. Drafting of optimal treatment scheme entailed use of long-acting drugs that ensure 24-hour control of blood pressure with a single or double medication per day thus making it more convenient for the patients and enhancing adhere to long-term treatment.

Single agent therapy with one of the three dugs – Amlodipine (5 mg/day), Lisinopril (10 mg/day) or Hydrochlorothiazide (25 mg/day) – was used for cost estimation of treatment of I degree HTN with moderate risk.

Single agent therapy with one of antihypertensive drug – Amlodipine (10 mg/day) or Lisinopril (20 mg/day) or combination of the two with average therapeutic dose – was also used for cost estimation of treatment of II degree HTN with moderate risk.

One combined therapy with maximum number of drugs including 2 antihypertensive drugs, statin and antiaggregant in average doses was used for cost estimation of treatment of HTN patients with I, II and III degrees with high and extremely high risk (Table 5).

Table 5. Treatment schemes used for cost estimation of HTN treatment

	With moderate CVC risk (I, II degree HTN)		**With high and extremely CVC risk (I, II, III degree HTN)**	
	Drug name	Dose	Drug name	Dose
I degree HTN	1. Amlodipine 2. Lisinopril 3. Hydrochlorothiazide	5 mg/day 10 mg/day 25 mg/day	Lisinopril + Amlodipine + Acetylsalicylic acid + Atorvastatin	10 mg/day 10 mg/day 100 mg/day 10 mg/day
II degree HTN	1. Amlodipine 2. Lisinopril 3.Lisinopril+ Amlodipine	10 mg/day 20 mg/day 10 mg/day 5 mg/day		

- **Estimated cost of medicinal treatment schemes using the cheapest INN generics and generics with brand names.**

Cost of treatment of the Ist degree HTN with moderate risk using the cheapest Amplodipine generic per person per year was estimated to be 230 KGS, Hydrochlorothiazide – 650 KGS and the cheapest Lisinopril generic – 1997 KGS.

Drug therapy using generics with brand names significantly increases the cost of treatment. For example, the cost of single agent therapy with Amlodipine using brand analogue is 15 times higher than using the cheapest INN generic and sums up to 3468 KGS.

Estimated cost of treatment of II degree HTN with moderate risk differs significantly depending on selected dugs when the cheapest generics are used. Hence, treatment cost of 1 patient per year with Amlodipine is 267 KGS and with Lisinopril it is 3990 KGS.

Treatment of II degree HTN with moderate risk using brand name generics is more expensive just like similar treatment of I degree HTN. For example, single agent therapy with brand analogue Amplodipine costs 20 times more than with cheapest INN generic and amounts to 5475 KGS per patient per year.

Cost of combined treatment of II degree HTN with moderate risk per patient per year (following the scheme Amlodipine + Lisinopril) using the cheapest generics amounts to 2227 KGS which is 3 times less than treatment using brand names which amounts to 6753 KGS (Table 6).

Table 6. Cost of treatment of 1 HTN patient with moderate risk per year

Drugs	Cost per 1 patient per year using cheapest generics (KGS)	Cost per 1 patient per year using generics with brand names (KGS)	Difference in cost of treatment
I degree HTN with moderate risk			
1. Amlodipine 5 mg	**230**	**3 468**	15,1
2. Hydrochlorothiazide 25 mg	**650**	**2 811**	4,3
3. Lisinopril 10 mg	**1 997**	**3 285**	1,6
II degree HTN with moderate risk			
1. Amlodipine 10 mg	**267**	5 475	20,5
2. Lisinopril 20 mg	**3 990**	5 201	1,3
3. Lisinopril 10 mg + Amlodipine 5 mg	**2 227**	6 753	3,0

Estimated cost of treatment of HTN of all degrees with high and extremely high risk per patient per year using the cheapest generics is 7 154 KGS while use of generics with brand names pursuing the same scheme raises the cost twofold and amounts to 15 294 KGS per patient per year (Table 7).

Table 7. Cost of treatment of 1 HTN patient with high and extremely high risk per year following the scheme

Treatment scheme	Cost per 1 patient per year using cheapest generics (KGS)	Cost per 1 patient per year using generics with brand names (KGS)	Difference in cost of treatment
HTN with high and extremely high risk (I, II, III degrees)			
Amlodipine 10 mg + Lisinopril 10 mg + Acetylsalicylic acid 100 mg + Atorvastatin 10 mg	**7154**	**15294**	**2,1**

- **Estimated cost of HTN treatment following 3 scenarios of patient coverage: 4.1%, 6.1% and 34.1% of HTN patients in adult population**

Estimated cost of treatment of Ist degree HTN patients with moderate risk ranges from 1.24 million KGS to 10.8 million KGS per year provided that all registered HTN patients (4.1% of adult population) are covered. Use of generics with brand names increases the cost of treatment to 18.7 million KGS and 17.7 million KGS accordingly. Cost of combined treatment scheme for II degree HTN with moderate risk ranges from 12.7 million KGS (cheapest generics) to 38.7 million KGS (generics with brand names). Estimated cost of treatment of HTN with high and extremely high risk ranges from 975 million KGS (cheapest generics) to 2.08 billion KGS per year (Table 8).

Table 8. Cost of HTN treatment with moderate, high and extremely high risk provided that all registered patients are covered – 4.1% of adult population[12]

Drugs	Cost per year/coverage of 4.1% of adult population (registered patients in 2013)	
	Cheapest generics (KGS)	Generics with brand names (KGS)
I degree HTN with moderate risk		
1. Amlodipine 5 mg	1 241 166,3	18 714 628,8
2. Hydrochlorothiazide 25 mg	3 507 643,8	15 169 210,4
3. Lisinopril 10 mg	10 776 561,1	17 727 092,2

[12] 4.1% of adult population in Kyrgyzstan is the quantity indicator reflecting the number of HTN cases registered in 2013 and baseline indicator from Indicator Package of Den Sooluk Program.

II degree HTN with moderate risk		
1. Amlodipine 10 mg	1 530 869,4	31 391 423,0
2. Lisinopril 20 mg	22 877 037,1	29 820 418,5
3. Lisinopril 10 mg + Amlodipine 5 mg	12 768 712,2	38 718 955,2
HTN with high and extremely high risk (I, II, III degrees)		
Amlodipine 10 mg + Lisinopril 10 mg + Acetylsalicylic acid 100 mg + Atorvastatin 10 mg	975 080 552,1	2 084 551 574,5

Providing coverage of 6.1% of adult population estimated cost of treatment of I degree HTN patients with moderate risk would range from 1.85 million KGS to 16.08 million KGS per year. Use of generics with brand names increases the cost of treatment to 27.9 million KGS and 26.45 million KGS accordingly. Cost of combined treatment scheme for II degree HTN with moderate risk ranges from 19.05 million KGS (cheapest generics) to 57.8 million KGS (generics with brand names) per year. Estimated cost of treatment of HTN with high and extremely high risk ranges from 1.45 billion KGS (cheapest generics) to 3.11 billion KGS per year (Table 9).

Table 9. Cost of HTN treatment with moderate, high and extremely high risk provided that all registered patients are covered – 6.1% of adult population[13]

Drugs	**Cost per year/coverage of 6.1% of adult population (target indicator of HTN patients coverage, Den Sooluk)**	
	Cheapest generics (KGS)	**Generics with brand names (KGS)**
I degree HTN with moderate risk		
1. Amlodipine 5 mg	1 852 035,6	27 925 475,4
2. Hydrochlorothiazide 25 mg	5 234 013,6	22 635 095,6
3. Lisinopril 10 mg	16 080 500,1	26 451 899,3
II degree HTN with moderate risk		
1. Amlodipine 10 mg	2 284 322,9	46 841 453,3
2. Lisinopril 20 mg	34 136 511,2	44 497 241,8
3. Lisinopril 10 mg + Amlodipine 5 mg	19 053 135,4	57 775 403,5

[13] 6.1% of adult population in Kyrgyzstan is the target indicator reflecting the number of registered HTN cases from the Indicator Package of Den Sooluk Program

HTN with high and extremely high risk (I, II, III degrees)		
Amlodipine 10 mg + Lisinopril 10 mg + Acetylsalicylic acid 100 mg + Atorvastatin 10 mg	1 454 989 475,5	3 110 512 865,2

Providing coverage of 34.1% of adult population estimated cost of treatment of I degree HTN patients with moderate risk would range from 10.32 million KGS to 89.62 million KGS per year. Use of generics with brand names increases the cost of treatment to 155.69 million KGS and 147.43 million KGS per year accordingly. Cost of combined treatment scheme for II degree HTN with moderate risk ranges from 103.7 million KGS (cheapest generics) to 314.7 million KGS (generics with brand names) per year. Estimated cost of treatment of HTN with high and extremely high risk ranges from 8.1 billion KGS (cheapest generics) to 17.33 billion KGS per year (Table 10).

Table 10. Cost of HTN treatment with moderate, high and extremely high risk provided that all registered patients are covered – 34.1% of adult population[14]

Drugs	**Cost per year/coverage of 34.1% of adult population (HTN incidence rate according to Interepid data)**	
	Cheapest generics (KGS)	**Generics with brand names (KGS)**
I degree HTN with moderate risk		
1. Amlodipine 5 mg	10 322 816,5	155 650 120,2
2. Hydrochlorothiazide 25 mg	29 173 177,1	126 162 770,5
3. Lisinopril 10 mg	89 628 976,4	147 436 748,8
II degree HTN with moderate risk		
1. Amlodipine 10 mg	12 442 506,5	255 141 285,3
2. Lisinopril 20 mg	185 938 580,5	242 372 570,7
3. Lisinopril 10 mg + Amlodipine 5 mg	103 780 756,6	314 697 552,4
HTN with high and extremely high risk (I, II, III degrees)		
Amlodipine 10 mg + Lisinopril 10 mg + Acetylsalicylic acid 100 mg + Atorvastatin 10 mg	8 109 777 590,7	17 337 285 221,1

[14] Interepid study findings suggest that incidence rate of hypertension in the Kyrgyz Republic is 34.1% of adult population

4.4. Possible mechanisms of free or reimbursed drug provision for HTN treatment

Option 1. Including statins into the ADP

This option will require significant increase in the level of ADP funding which in turn will imply revision of implementation mechanisms of this program with focus on improved targeting.

According to provisional estimates, amount of reimbursement for 1 tablet will be 12.91 KGS for the 1st level (at the rate of average base price) if Atorvastatin is included into the ADP at 50% reimbursement level. MHIF reimbursement amount per 1 person per year will come to 4712.2 KGS.

Estimated data suggest that the total number of registered HTN patients (I, II, III degrees) with high and extremely high CVC risk is 136 279 people. All of them are subjected to mandatory therapy with statins. If all these patients are provided with statins under the ADP then the annual reimbursement amount would come up to 642.17 million KGS.

	Reimbursement amount per 1 tablet (KGS)	**Reimbursement amount per year per 1 person (KGS)**	**Estimated number of registered HTN patients with high and extremely high risk – 136 279 persons X Reimbursement amount per year per 1 person (KGS)**
Atorvastatin 10 mg	**12,91**	**4712,2**	**642 173 903,8**

***Note:** Forecasted funding level of MHI ADP for 2014 is only 182 812 725 KGS. In light of the aforementioned proposal it becomes necessary to revise overall MHI ADP policy for the future.*

Option 2. Including HTN of all degrees with high and extremely high risk into the drug package of SGBP

Given than under the first option only insured patients are eligible for exempt drugs it is feasible to examine the possibility of subsuming HTN patients with high and extremely high risk into the exempt category at outpatient level under the State-guaranteed Benefit Package. At this stage SGBP covers 4 conditions with different categories of patients irrespective of insurance status.

A prerequisite for this would be defining the drugs for full reimbursement from SGBP drug package and specifying the dispensing practice of these drugs per patient per year.

The above cost estimation of combined treatment of HTN with high and extremely high risk using the cheapest generics was **975.08 million KGS per year** provided that all registered HTN patients were covered (4.1% of adult population).

However, the 2014 projected financing from the republican budget funds for subsidized pharmaceutical provision in the framework of State Benefits Program is 23 272 400 som only.

Inclusion of this category of patients into the SGBP drug package would require earmarked allocation of additional funds in the Single Payer system budget for 2015 with respective modification of SGBP to add hypertensive disease with high and extremely high risk to the five currently monitored conditions.

5. CONCLUSIONS AND CONSIDERATIONS

1. Difference between the official data on HTN incidence rate and findings from the two studies with strict methodology indicates the shortfalls in the system of HTN detection, registration and treatment. Hence it is quite logical that coverage of patients with HTN treatment programs was incomplete.

2. Despite the existing drug benefit programs, high expenditures for outpatient treatment remain the main cause of high financial burden for patients with hypertension. This draws from the restricted nature of exemptions for relevant drugs and insufficient coverage of HTN patients. Research data show that in Kyrgyzstan more than 1.2 million people have elevated blood pressure. In 2013, in the context of existent drug benefit program 120 thousand HTN patients had the opportunity to buy drugs at reduced price (by 10%) throughout the year. Yet, the scope of prescribed drugs is limited and does not allow patients to ensure continuous and effective blood pressure control through use of drugs subsidized by the government. The aforementioned data showing that MHI ADP provides a patient with drugs for HTN treatment for only 2 months on average out of annual demand indicate insufficient level of drug provision for this group of patients.

3. Cost estimations of medicinal treatment schemes for HTN with different degrees and CVC risk showed that cost of treatment depends heavily on the price of used drug (generic with INN or generic with brand name). Although the availability of large quantity of generic drugs in the Kyrgyz market assumes enhanced choice and, in some cases, improved adherence to drug intake there is still the need to further strengthen price regulation with a view of improving access to antihypertensive drugs and due to the wide price range for these drugs. Results of cost estimation of HTN treatment in Kyrgyzstan for individual patients and using three scenarios of HTN patient coverage varied markedly. And the causes are as follows: i) dependence on medicinal treatment scheme reflecting clinical aspects of disease; ii) availability of large quantity of generic drugs in the pharmaceutical market with wide price range.

4. The following results were obtained from cost estimation of HTN treatment per patient per year:

4. 1. For HTN patients with **moderate risk** of cardio-vascular complication the cost varies:

i. **for single agent therapy,** which is used for I and II degree HTN, from 230 KGS (cheapest generics) to 5475 KGS (brand names) per patient per year;
ii. **for combined therapy**, which is used for II degree HTN, from 2227 KGS (cheapest generics) to 6753 KGS (brand names) per year.

Cost of combined treatment using statins for patients with **high and extremely high risk** of cardio-vascular complications varies:

iii. when using **cheapest generics** it amounts to 7154 KGS per patient per year;
iv. when using **brand names** – 15294 KGS per patient per year.

4.2. Estimated cost of HTN treatment with coverage of registered patients being **4.1% of adult population**:

For patients with **moderate risk** of complications

i. cost of **single agent therapy** for I and II degree HTN ranged from 1.24 million KGS to 22.87 million KGS when cheapest generics were used;
ii. cost of **combined therapy** for II degree HTN ranged from 12.76 million KGS (cheapest generics) to 19.05 million KGS (brand names) per year.

For patients with high and extremely high risk of complications the cost varies:
iii. when using **cheapest generics** it amounts to 975.08 million KGS per year;
iv. when using **brand names** it amounts to 2.08 billion KGS per year.

5. Use of statins for HTN treatment demands close attention especially in patients with high and extremely high CVC risk. Low countrywide consumption and limited availability of statins in retail pharmacy chains with concentration only in central districts and cities indicate a need to improve access to statins for HTN patients. High price of statins as compared to prices of other components used for antihypertensive treatment and geographical barriers related to physical accessibility of statins are noted among other possible reasons.

It is possible that low consumption of statins by patients with high risk of complications can be attributed primarily to uncommon prescription of statins by doctors which, in turn, entails demand drawdown for these drugs and respectively deficiency in the pharmacy chain and lack of competition that could reduce prices for statins.

In this context it is advised to explore to what extent the doctors are aware about the role of statins in managing HTN patients with high CVC risk.

In all accounts access to statins for patients who need them significantly increases cost of treatment of HTN patients with complications. Inclusion of statins into drug benefit programs subsidized by the government would require considerable increase in funding level.

ANNEX 1

Cost of treatment for moderate (I and II degree), high and extremely high risk HTN of all degrees with the cheapest generic drugs

ug	Daily dose	Unit price (KGS)	Cost of 1 patient per month (30 days), KGS	Cost of 1 patient per year (365 days), KGS	Annual cost/ HTN incidence of 4.1%/KGS	Annual cost/ HTN incidence of 6.1%/KGS	Annual cost/HTN incidence of 34.1%/KGS
I degree HTN – moderate risk							
Amlodipine	5 mg	**0,63**	**19**	**230**	1 241 166,3	**1 852 036**	**10 322 817**
Hydrochlorotiaside	25 mg	**1,78**	**53,5**	**650**	3 507 644	**5 234 014**	**29 173 177**
Lisinopril	10 mg	**5,47**	**164**	**1997**	10 776 561	**16 080 500**	**89 628 976**
II degree HTN – moderate risk							
Amlodipine	**10 mg**	**0,73**	**22**	**267**	**1 530 869**	**2 284 323**	**12 442 507**
Lisinopril	**20 mg**	**10,93**	**328**	**3990**	**22 877 037**	**34 136 511**	**185 938 581**
Lisinopril +	10 mg	5,47					
Amlodipine	5 mg	0,63					
Cost of treatment scheme		**6,1**	**183**	**2227**	12 768 712	19 053 135	103 780 757
All degrees HTN – high and extremely high risk							
Amlodipine +	10 mg	0,73					
Lisinopril +	10 mg	5,47					
ASA +	100 mg	0,06			975 080 552	1 454 989 475	8 109 777 591

Atorvastatin	10 mg	13,33					
Cost of treatment scheme		**19,6**	**588**	**7154**			

Cost of treatment for moderate (I and II degree), high and extremely high risk HTN of all degrees with generic drugs prescribed under the brand names

Drug	Daily dose	Unit price (KGS)	Cost of 1 patient per day/KGS	Cost of 1 patient per year/KGS	Annual cost/ HTN incidence of 4.1%/KGS	Annual cost/ HTN incidence of 6.1%/KGS	Annual cost/ HTN incidence of 34.1%/KGS
I degree HTN – moderate risk							
Amlodipine	**5мг**	**9,5**	**285**	**3468**	**18 714 629**	**27 925 475**	**155 650 120**
Hydrochlorotiaside	**25мг**	**7,7**	**231,5**	**2811**	**15 169 210**	**22 635 096**	**126 162 770**
Lisinopril	**10мг**	**9**	**270**	**3285**	**17 727 092**	**26 451 899**	**147 436 749**
II degree HTN – moderate risk							
Amlodipine	10 мг	15	450	5475	31 391 423	46 841 453	255 141 285
Lisinopril	20 мг	14,25	427,5	5201	29 820 418	44 497 242	242 372 571
Lisinopril +	10 мг	9					
Amlodipine	5 мг	9,5					
		18,5	**555**	**6753**	19 053 135	57 775 403	314 697 552
All degrees HTN – high and extremely high risk							
Amlodipine +	10 мг	15					
Lisinopril +	10 мг	9					
ASA +	100мг	2					
Atorvastatin	10 мг	15,9					
		41,9	**1257**	**15294**	2 084 551 575	3 110 512 865	17 337 285 221