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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

(DRAFT)

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List of Abbreviations

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

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] survey 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

[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.

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 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 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 hypertensive disease based on approved clinical guidelines of HD treatment in adults. Estimations can be used as grounds for consideration of mechanisms ensuring free provision of antihypertensive drugs to incentivize improved HD diagnostics and uninterrupted control.

2. Research goal and objectives

Goal of this research is to estimate cost of treatment of hypertensive disease (HD) as consistent with clinical guideline for HD 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 HD patients with drugs?
2. Cost analysis of main drugs used for HD treatment in Kyrgyzstan.
3. What is the cost of medicinal treatment of HD as consistent with clinical guideline for HD treatment with due consideration of incidence rate for different categories of patients (including the risk of alleviated blood pressure, cardio-vascular complications and co-morbidities)?

[3] HPAC: CIHS, NHA – 2009
[4] HPAC: National Drug Policy Analysis, 2007-2010
[5] HPAC: Health system effectiveness in hypertensive disease control in Kyrgyzstan, 2007

3. Methodology

3.1 Analysis of drug benefit programs coverage of HD patients

During the discussion of issues related to cost estimation of medicinal treatment of HD 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 HD patients. To verify this opinion it was decided to analyze the pattern of drug use by HD patients and the coverage of HD patients with indicated program. The analysis was reposed on data from MHIF database.

3.2 Cost analysis of main drugs used for HD 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 hypertensive disease treatment were used to estimate the cost of medicinal treatment – using the price of the cheapest generics with INN available in the market 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 hypertensive disease 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 thus 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 advertized 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 affect on financial burden and adherence to uninterrupted intake of medicines. The situation is

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

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 hypertensive disease

Basic approached used for cost estimation of medicinal treatment of hypertensive disease among the Kyrgyz population

Considering incidence of hypertensive disease in January 2013, the number of officially registered patients with HD was 4.1% of adult HD 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 HD 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 HD 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 HD detection, registration and treatment. Nonetheless, expected outcomes of Den Sooluk program presume increased number of detected HD 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 HD patients with treatment was set by Den Sooluk at 6.1% of adult population for the year 2016.

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

- Stratification of HD patients by additional risk of cardio-vascular complications to define HD 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 AH patients". This means that when providing treatment to AH 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 HD patient treatment.

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

Approved clinical guideline for HD treatment determines treatment schemes of HD 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 HD patients 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 HD with low risk of cardio-vascular complications were undertaken.

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

Cost estimation of medicinal treatment of HD 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 HD treatment in adult population (2010).

[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

4. Findings

4.1. Analysis of HD 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 HD 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 hypertensive disease 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 HD 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 HD 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, HD patients who receive drugs under this program are provided with necessary drugs only for 2 months a year at max. Mindful that HD 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 HD treatment

Estimation of HD treatment cost was done through calculation of optimum combinations of 5 drugs of which 3 drugs are the first-line drugs for HD 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.

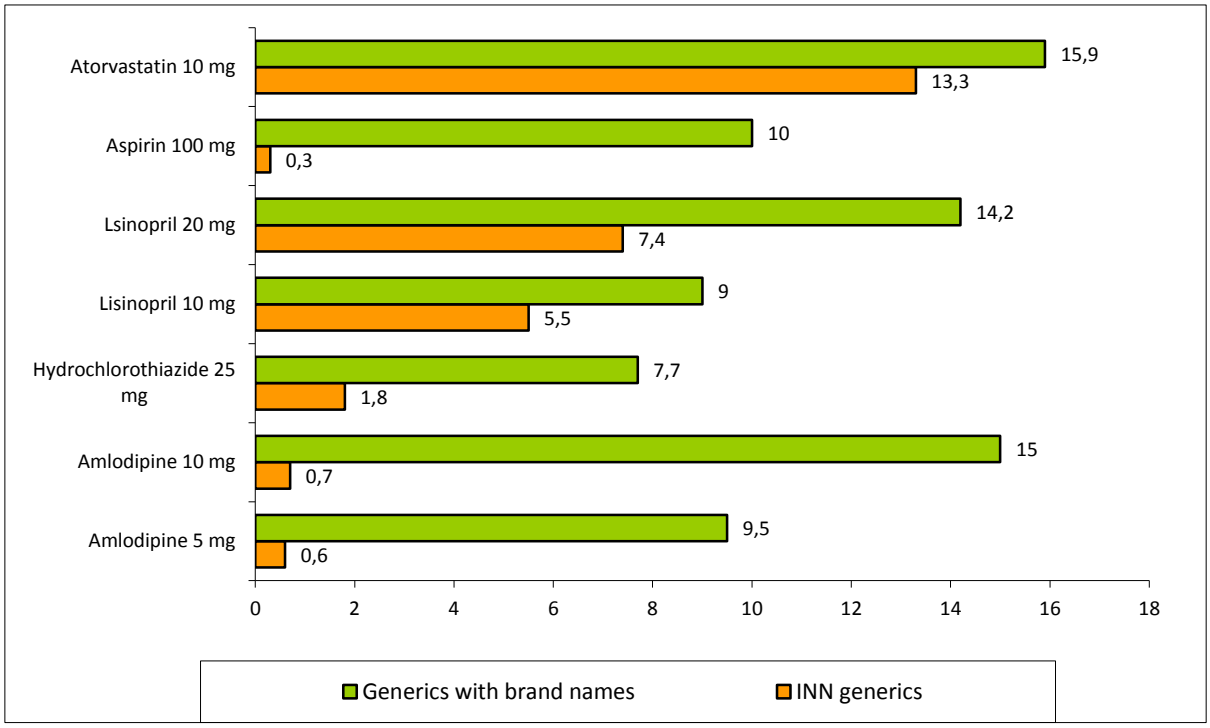
Drug prices were obtained from the DDPME database of wholesale prices for drugs as of September 2013.

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 HD 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 hypertensive disease

- HD incidence structure by degrees

Cost estimation of HD treatment with account of incidence rate entailed used 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 HD 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 hypertension	**140-159**	**90-99**
II degree hypertension	**160-179**	**100-109**
III degree hypertension	**≥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):

HD	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 HD patients by complementary risk of cardio-vascular complications

Data from international clinical guidelines for HD treatment and findings from studies on stratification of HD patients by CVC risk were used to stratify HD 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 HD patients 17% have moderate CVC risk and 83% have high and extremely high risk of CVC. All patients with III degree HD 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 HD patients by degrees and risks was utilized for estimation of HD patients by CVC risks in the KR.

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

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

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

Table 1

Extrapolation of HD incidence structure by CVC risk

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

Therefore, all 197 798 patients with III degree AH as well as the majority of HD 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 HD incidence structure as percent of total number of HD patients obtained from Interepid findings (34.1% of adult population in the KR) (Table 2).

Table 2

Estimated number of HD patients, in %, by risk and blood pressure degree

	% of HD patients with moderate CVC risk	% of HD patients with high and extremely high CVC risk
I degree HD	44 882 (3.66%)	703 153 (57,34%)
II degree HD	47 687 (3.88%)	232 826 (19%)
III degree HD		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 HD patients identified by the Interepid study. The most prevalent group consists of patients with I degree AH 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 HD patients depending on CVC risk on condition of 100% patient coverage.

This structure of HD incidence by CVC risk was used to estimate the number of HD 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 HD patients (147 429 people) which is the baseline indicator from Den Sooluk program reflecting registered number of HD patients.

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

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

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

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

- Define medicinal treatment scheme of HD 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 HD 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 hypertensive disease 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 HD 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 HD patients with different degrees of blood pressure elevations and CVC risk.

Recommendations from the approved protocol for HD 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 HD 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 HD 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 HD patients with I, II and III degrees with high and extremely high risk. (Table 5).

Table 5

Treatment schemes used for cost estimation of HD treatment

	With moderate CVC risk (I, II degree HD)		**With high and extremely CVC risk (I, II, III degree HD)**	
	Drug name	Dose	Drug name	Dose
I degree HD	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 HD	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 HD 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 HD 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 HD with moderate risk using brand name generics is more expensive just like similar treatment of I degree HD. 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 HD 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 HD 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 HD 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 HD 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 HD 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 HD 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
HD 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 HD treatment following 3 scenarios of patient coverage: 4.1%, 6.1% and 34.1% of HD patients in adult population

Estimated cost of treatment of Ist degree HD patients with moderate risk ranges from 1.24 million KGS to 10.8 million KGS per year provided that all registered HD 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 HD 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 HD 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 HD 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 HD 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
II degree HD 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
HD 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 HD 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 HD 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 HD with high and extremely high risk ranges from 1.45 billion KGS (cheapest generics) to 3.11 billion KGS per year (Table 9).

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

Table 9

Cost of HD 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 HD patients coverage, Den Sooluk)	
	Cheapest generics (KGS)	Generics with brand names (KGS)
I degree HD 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 HD 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
HD 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 HD 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 HD 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 HD with high and extremely high risk ranges from 8.1 billion KGS (cheapest generics) to 17.33 billion KGS per year (Table 10).

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

Table 10
Cost of HD 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 (HD incidence rate according to Interepid data)	
	Cheapest generics (KGS)	Generics with brand names (KGS)
I degree HD 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 HD 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
HD 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

4.4. Possible mechanisms of free or reimbursed drug provision for HD 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 HD patients (I, II, III degrees) with high and extremely high CVC risk is 136 279 people. All of them are subjected to

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

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 HD 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 HD 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 HD 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 HD with high and extremely high risk using the cheapest generics was **975.08 million KGS per year** provided that all registered HD patients were covered (4.1% of adult population).

***Note:** Forecasted level of SGBP funding for 2014 from the republic budget is 23 272 400 KGS.*

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 HD incidence rate and findings from the two studies with strict methodology indicates the shortfalls in the system of HD detection, registration and treatment. Hence it is quite logical that coverage of patients with HD 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 HD 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 HD 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 HD 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 HD 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 HD treatment in Kyrgyzstan for individual patients and using three scenarios of HD 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 HD treatment per patient per year:

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

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

ii. **for combined therapy**, which is used for II degree HD, 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 HD 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 HD ranged from 1.24 million KGS to 22.87 million KGS when cheapest generics were used;

ii. cost of **combined therapy** for II degree HD 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 HD 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 HD 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 HD patients with high CVC risk.

In all accounts access to statins for patients who need them significantly increases cost of treatment of HD 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 HD of all degrees with the cheapest generic drugs

Drug	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/HD incidence of 4.1%/KGS	Annual cost/HD incidence of 6.1%/KGS	Annual cost/HD incidence of 34.1%/KGS
I degree HD – 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 HD – 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 + Amlodipine **Cost of treatment scheme**	10 mg 5 mg	5,47 0,63 **6,1**	**183**	**2227**	12 768 712	19 053 135	103 780 757
All degrees HD – high and extremely high risk							
Amlodipine + Lisinopril + ASA + Atorvastatin **Cost of treatment scheme**	10 mg 10 mg 100 mg 10 mg	0,73 5,47 0,06 13,33 **19,6**	**588**	**7154**	975 080 552	1 454 989 475	8 109 777 591

Cost of treatment for moderate (I and II degree), high and extremely high risk HD 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/HD incidence of 4.1%/KGS	Annual cost/HD incidence of 6.1%/KGS	Annual cost/HD incidence of 34.1%/KGS
I degree HD – 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 HD – 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 HD – 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