Estimated Cost for Risk Based Management of Cardiovascular Diseases in Primary Health Care in Nepal by Using Total Risk Approach

Anu Aryal

A thesis

submitted in partial fulfilment of the

requirements for the degree of

Master of Public Health

University of Washington

2017

Committee:

Rachel Nugent

Joseph Dieleman

Annette Fitzpatrick

Program Authorized to Offer Degree:

Global Health

University of Washington

Abstract

Estimated Cost for Risk Based Management of Cardiovascular Diseases in Primary Health Care in Nepal by Using Total Risk Approach

Chair of the Supervisory Committee:

Prof. Rachel Nugent

Department of Global Health

Background: We estimated the direct medical cost of primary prevention of cardiovascular diseases (CVD) in the primary health care center (PHCC) using the GLOBAL HEARTS treatment protocols for risk based management of CVD.

Method: We took the Ministry of Health's perspective, and used a one-year time horizon. Cost for human resources and laboratory tests were estimated in the context of Nepal, while international drug prices obtained from Management Sciences of Health (MSH) and local prices for non study related drugs from Nepal's Logistic Management division (LMD) were used in estimating local drug prices. The cost estimates are presented in both current Nepali rupees (NPR) and current US dollars (2017).

Results: The estimated cost to provide CVD primary prevention for each patient was $3.05 for the first visit and an additional $0.09 for patients with risk <10%, $4.35 for patients with risk 10-20% with high blood pressure (HBP), $25.46 for patients with risk 10-20% with high cholesterol, $33.04 for patients with risk 20-30%, $37.35 for patients with risk >30% and an additional $38.04 cost for management of those with diabetes. For a primary health care center

with a population of 10,000, the estimated cost to screen and treat 50% of eligible patients was $12 per case and $1 per capita. The total annual cost varied from $5,000 at 25% coverage to as high as $15,000 at 75% coverage.

Conclusion: Providing CVD prevention services at PHCCs is inexpensive. Along with the financial resources, health facilities will also need higher capacity for human resource, logistic management and laboratory services.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

CDC	Centers for Disease Control and Prevention
CVD	Cardiovascular Diseases
DALY	Disability Adjusted Life Years
EDP	External Development Partner
IHD	Ischemic Heart Disease
LMD	Logistic Management Division
MoH	Ministry of Health
MSH	Management Science for Health
NCD	Non-communicable Diseases
NPR	Nepalese Rupee
PEN	Package of Essential Non-communicable diseases
PHCC	Primary Health Care Center
SEAR	South East Asia Region
WHO	World Health Organization
USD	United States Dollar

I. BACKGROUND

Cardiovascular Diseases Globally

Cardiovascular diseases are the leading cause of disability and death globally (1)(2). The estimates from the Global Burden of Disease study show that the burden of CVD is increasing worldwide. The disability adjusted life years (DALY) due to CVD increased by 33.7% from 1990 to 2015 (3). In 2015 alone, the two most common cardiovascular events: ischemic heart disease (IHD) and stroke, led to approximately 15 million deaths worldwide (2). The 30 days' case fatality rate after a coronary vascular event is 25% in people aged 40 years and is as high as 50% for people aged 70 years (4). It is projected that IHD and stroke will result in 17.8 million annual deaths by the year 2030 (5).

High blood pressure and blood glucose are the major metabolic risk factors for cardiovascular diseases (6). An increase in systolic blood pressure of 10mmgHg results in two fold increased risk of stroke and ischemic heart disease in adults aged 35-44 years. In the same age group, the risk of stroke and IHD is 20% higher with each 1mmol/L increase in fasting plasma glucose (6). Other metabolic risk factors for CVD are high cholesterol and obesity (6). Management of these risk factors is a major prevention strategy for addressing CVD to reduce mortality and morbidity from these conditions. In this study, we estimated the direct cost of CVD case management in a primary health care setting. We included the cost of screening, treatment, and follow up for patients presenting at primary health care centers in Nepal.

Cardiovascular Diseases in Nepal

Cardiovascular diseases are the number one cause of death in Nepal with approximately 44 thousand deaths attributed to them in 2015 (7). Data from the recent STEPs survey revealed that

25.7% of the population over 15 years in Nepal have high blood pressure, 3.6% have high fasting glucose, and 22.7% have elevated total cholesterol.

The Government of Nepal has adopted WHO's global target of a 25% reduction in mortality from non- communicable diseases including CVD, cancers, diabetes and chronic respiratory diseases, by 2025 (8). In addition to population based interventions in prevention of NCDs, plans are also in place to prevent ischemic heart disease and stroke by managing 50% of eligible patients with drug therapy and counselling during the same period.

Nepal is planning to implement a Package of Essential Noncommunicable (PEN) Disease protocols for management of noncommunicable diseases (NCDs) in primary health care (8). The PEN package, launched by the World Health Organization (WHO) outlines essential interventions for four major NCDs: cardiovascular disease, cancer, diabetes and chronic respiratory disease. A more specific program tailored for cardiovascular diseases (including diabetes) prevention and management for low resource settings is Global HEARTS. Launched by WHO and CDC in 2016, Global HEARTS includes most of the PEN protocols for risk based management for CVD prevention, and offers more specific training and monitoring support to the implementing countries. Nepal is planning to pilot PEN in two districts, and also is a selected demonstration site for the Global HEARTS program.

The Global HEARTS program promotes management of cases based on "total cardiovascular risk" approach for CVD prevention in primary health care. Total cardiovascular risk is the probability a person will have a cardiovascular events such as stroke or ischemic heart disease over a 10 year period (4). It is calculated by using a CVD risk prediction tool, developed by WHO and the International Society of Hypertension (ISH), that estimates the risk profile based on individual

characteristics of patients including age, sex, blood pressure, smoking status, fasting blood glucose and cholesterol (4).

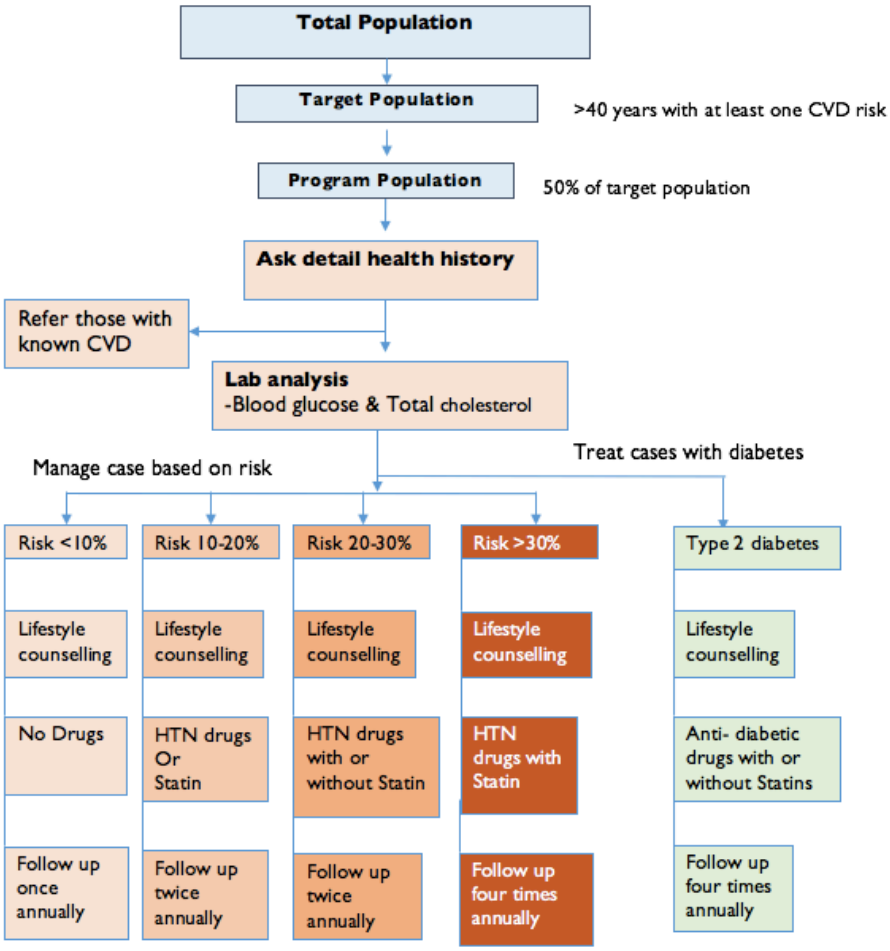

Figure 1: Summary of the case management protocol used in this study

It divides the adult population into 4 absolute risk categories: <10%, 10-20%, 20-30% and >30% risk of an event within 10 years. WHO has developed population based risk profiles for 14 distinct regions around the world, and the exercise is ongoing for preparing such profiles for each country (4) . Figure 1 shows the risk based management scenario used in the study based on the Global HEARTS technical package.

II. METHODS

We estimated the cost from the perspective of the Ministry of Health (MoH), Nepal, as the payer for public primary health care centers in Nepal. A one-year time horizon was used, and cost was presented both in current Nepali rupees (NPR) and current US Dollars (USD 2017). The exchange rate of 101.9 (1 USD = 101.9 NPR) was used for currency conversion (https://www.oanda.com) into 2017 USD price. We only estimated direct medical cost, as another similar study demonstrated that 97% of the program cost is direct service cost (9). We estimated the cost of each inputs such as human resource time, laboratory analysis and drugs used. We didn't include capital equipment cost. Cost results were aggregated as cost per case and cost per capita.

A hypothetical primary health care center serving a population of 10 thousand people was taken as a base case for the study. Age and sex distribution of the population was calculated using national population age and sex distribution data from census 2011(10). The proportion of adults 40 years and above, with at least one risk factor for noncommunicable diseases, as identified in the Nepal STEPS survey 2013(11), was used to estimate the target population eligible for screening services. The coverage of the population at this facility was assumed to be 50% following the target set by the Government of Nepal in the NCD action Plan. We also did a sensitivity analysis with varying coverage of 25%, 50% and 75%. Due to a lack of a population-wide CVD absolute risk distribution data from Nepal, we used the population risk profile for WHO South East Asia region C, for estimates of risk distribution in Nepal.

Treatment protocols from the Global HEARTS package(12) were used to assess services and medicines needed for each risk category. For individuals with less than 10% risk, only screening and lifestyle counselling was provided in the estimate, while for other categories medical treatment was required. An expert from WHO was consulted to determine the daily average dose of the

drugs. Among the list of recommended drugs, the proportion of patients using each drug was derived from the NCD costing tool (13). NCD costing tool was developed by WHO in 2012 as one of the implementation tools for PEN disease interventions for low resource setting, to be used for financial resources forecasting at national and sub-national level (14).

To obtain the local price of the CVD drugs, we initially reached out to the Logistic Management Division (LMD) within the Department of Health Services in Nepal, but the bidding process for selection of NCD drugs was then taking place and costs were not known at the time of this analysis. We then estimated the price of those medications using the Management Science for Health (MSH) international medical products price guide (15). The specific process we used for estimating the price of CVD drugs included several steps. First, we downloaded the notice of intent for a variety of drug purchases made publicly available by LMD from their website. The price of those drugs paid by the government was then compared with the international buyer median price of same drugs, and a ratio of those two prices were calculated. We identified 26 such drugs purchased by the Nepalese government which, after comparison, were found on average to be half the price of international drug prices (mean 0.5, 95% CI 0.36, 0.63). The factor of 0.5 was then used to estimate the price of the CVD drugs used in our study. A sensitivity analysis was done with lowest and highest price of drug using lowest and highest estimates from the 95% confidence interval.

The Nepal government's civil servant salary was used for human resource costs of physician and nurses. A working year of 265 working days, and 8 hours of work each day, was used to calculate per minute price of human resources. First visit was assumed to take 10 min of provider's time, lifestyle counselling was assumed to take 5 minutes, while subsequent follow up visits for risk <10% was assumed to be 3 minutes, 10-20% was assumed to be 4 minutes, and for all above >20 risk including patients with type 2 diabetes was assumed to be 5 minutes.

The laboratory analysis of specific CVD assays (see table 1) varies from facility to facility in Nepal without a central procurement system like that one for the drugs. To estimate the laboratory costs, we contacted one primary health care center (PHCC), one district hospital, one zonal hospital and one tertiary hospital in Nepal to collect the actual cost charged for these analyses at their laboratories. For the study, we used the cost at lowest level of health facility whenever available. Laboratory technicians' time was not included in the costs since our assumption was that the laboratories were self sufficient, and the price reflected all costs involved in the analyses.

III. RESULTS

Table 1 shows laboratory cost at different levels of facilities in Nepal. Since, all laboratory analysis required in the Global HEARTS protocol are not performed in PHCCs in Nepal, we collected cost of those from different higher level facilities as well. Bhimad PHCC is the primary health care center, Tikapur hospital is district level hospital, Seti Zonal hospital is zonal hospital and Dhulikhel hospital is tertiary medical center. Moving from left to right, each facility is one level higher than the lower facility, and higher facilities serve as the referral unit for the lower level facilities. As the table suggests, laboratory analyses including cholesterol, urine ketone and serum potassium are not performed in the primary health care center. For the purpose of our study, we used the cost of laboratory analysis at the lowest health facility where the analysis was performed.

The laboratory test conducted for all patients screened are urine routine test, which includes urine glucose and urine protein test, blood glucose test and total cholesterol test, and they cost $0.39, $0.49 and $1.47 respectively. Urine ketone test is required for some patients with diabetes, and it

costs $1.47. Serum creatinine and serum potassium tests are only required for patients who are taking enalapril and they cost $1.96 and $2.96 respectively.

Table 1: Cost of different laboratory analysis by facilities

	Bhimad	Tikapur	Seti Zonal	Dhulikhel	Cost used in the study	
Laboratory tests	PHCC	hospital	hospital	hospital	NPR	USD
*Urine routine test	40	40	40	81	40	$0.39
Blood glucose	50	90	50	80	50	$0.49
Urine ketone	NA	NA	NA	150	150	$1.47
Serum Creatinine	150	150	140	150	150	$1.47
Total Cholesterol	NA	NA	200	200	200	$1.96
Serum Potassium	NA	NA	NA	300	300	$2.94

*Urine routine test includes urine glucose and protein test 1 USD= 101.9 NPR

All prices are in NPR unless mentioned otherwise

Table 2 shows the daily cost of different medications used for management of hypertension, diabetes and cholesterol used in our cost models. Insulin was found to be the most expensive drug at $0.078 per day, while atenolol was the least expensive costing only $0.003. Costs of other antihypertensive drugs except enalapril were also relatively cheaper compared to drugs for cholesterol management and glucose control. The cost of daily dose of enalapril was $0.009, amlodipine $0.005, and hydrochlorthiazide $0.004. Similarly, daily dose of glibenclamide can cost $0.008 and metformin can cost $0.039. Statins are relatively expensive compared to anti-hypertensive medications: cost of daily average dose of atorvastatin and simvastatin was $0.027 and $0.066 respectively.

Table 2: Daily cost of drugs for different conditions

Drugs	Average daily dose	Cost per day	
		NPR	US dollars
Medications for high blood pressure			
Amlodipine	10mg	0.52	$0.005
Atenolol	50mg	0.32	$0.003
Enalapril	10mg	0.96	$0.009
Hydrochlorthiazide	25mg	0.48	$0.004
Medications for high blood glucose			
Metformin	1500mg	3.99	$0.039
Glibenclamide	10mg	0.84	$0.008
Insulin Isophane	24 IU	7.95	$0.078
Medication for high cholesterol			
Atorvastatin	10mg	2.72	$0.027
Simvastatin	20mg	6.70	$0.066

1 USD= 101.9 NPR

Table 3 shows the incremental time required for health providers in delivering the services. This type of calculation is important in estimating the additional human resource need to manage patient load. At 50% coverage level with a PHC serving 10 thousand populations, on average physician's workload will increase by 2 hours per week, and nurse's workload will increase by 6 hours. Only one physician and one nurse is assumed to be employed in the facility, and it is consistent with the

Government of Nepal's staffing levels at PHCCs. This estimate assumed the patient workload is distributed equally throughout the year.

Table 3: Incremental time of health care providers in management of the additional cases

	Time per case/year (minutes)		Patients needing services annually	Total time/year for population	
	Physician	Nurse		Physician	Nurses
first visit	0	15	865	0	12970
risk <10%	0	3	566	0	1698
risk 10-20% with high BP	8	0	60	480	0
risk 10-20% with high cholesterol	10	0	60	600	0
risk 20-30%	10	0	52	520	0
risk >30%	20	0	77	1534	0
management of diabetic patients	20	0	29	587	0
Total additional time needed for a year (min)				3721	14668
Incremental time per week on average (hour)				2	6

Nurses responsible for first visit of all clients and follow up of risk <10%,

Physician responsible for treatment and follow up of all other cases

Table 4 shows the annual cost of the risk based management services per case by different risk types. Figure 1 provides more detail on how patient will move through the health system. In these estimates we assume that all clients arriving at the facility, regardless of their risk profile will receive new patient services which includes a medical history and complete clinical examination. An additional 5 minutes' time for counselling is also included in this visit. It is estimated to cost $0.45 each for such visit. Patients with known coronary vascular diseases like ischemic heart disease or stroke will be referred to next referral unit, as primary health care centers (PHCCs) are not equipped to manage those cases. The remaining clients who are not referred then will have

laboratory screening tests, which is estimated to cost $2.46 per case. Clients will then be categorized into five risk categories based on their results from history, examination, laboratory tests.

Additional to the new patient services in the first visit, each case with risk <10% is estimated to cost $0.009, as they only require one follow up visit annually. Managing those with risk 10-20% with high blood pressure is estimated to cost additional $4.35 annually, while those with risk 10-20% with high cholesterol are estimated to cost additional $25.46 per year as they require additional cholesterol tests during their follow up visits. Additional cost to manage patients with risk of 20-30% and risk >30% were estimated to be $33.04 and $37.35. Because of lack of data from the STEPS survey on co-morbidity of diabetes among these risk profiles, a separate calculation was done for managing cases with high blood glucose, which is additional $38.04 per case.

Table 4: Annual cost of treatment of various conditions

				Total cost per case	
Services	PHCC visit	Laboratory	Drugs	NPR	USD
First visit- history, physical exam	45.93		0	45.93	$0.45
First visit- laboratory screening	0.00	250.75	0	250.75	$2.46
plus additional cost for management of patients in each risk categories					
risk <10%	9.19	0	0	9.19	$0.09
risk 10-20% with high BP	31.71	0	411.72	443.43	$4.35
risk 10-20% with high cholesterol	39.64	400	2154.96	2,594.60	$25.46
risk 20-30%	39.64	760	2566.68	3,366.32	$33.04

risk >30%	79.28	1160	2566.68	3,805.96	$37.35
plus additional cost for					
management of diabetic patients	79.28	780	3017.12	3,876.39	$38.04

All prices are in NPR unless mentioned otherwise 1 USD= 101.9 NPR

Table 5 provides the annual cost of treatment at the population level for a PHCC serving a catchment area of 10 thousand people at 50% coverage rate. It is estimated to cost the PHCC around 1 million rupees ($9,936 USD) to provide the risk based management services in the facility. This only includes the direct service delivery cost. The average total cost per case per year is $11.49, and the cost per capita per year is estimated to be $0.99.

Table 5: Annual cost of treatment at population level (for a population of 10,000 people)

Services and treatment	**Unit cost (NPR)**	**Population needing services**	**Total Cost**	
			NPR	**USD**
first visit- history, physical exam	45.93	865	39,714	$1,240
first visit- laboratory screening	250.75	815	204,461	$6,381
risk <10%	9.19	566	5,198	$204
risk 10-20% with high BP	443.43	60	26,615	$348
risk 10-20% with high cholesterol	2,594.60	60	155728	$2,037
risk 20-30%	3,366.32	52	175,123	$2,346
risk >30%	3,805.96	77	291,859	$3,655
management of diabetic patients	3,876.39	29	113,789	$3,551
Total cost			NPR 1,012,486	$9,936

1 USD= 101.9 NPR

A sensitivity analysis was done to estimate the cost of varying drug prices and coverage. Table 6 shows the variation in cost per capita with different coverage rates and different drug prices. At the lowest drug price, the per capita cost ranges from $0.42 at 25% coverage rate, $0.84 at 50% coverage and $1.25 at 75% coverage. At the mean drug price, the per capita cost is $0.50 at 25% coverage rate, $0.99 at 50% coverage and $1.49 at 75% coverage. At the highest drug price, the per capita cost is $0.57 at 25% coverage rate, $1.14 at 50% coverage and $1.71 at 75% coverage. Per patient cost was most sensitive to changes in coverage rates.

Table 6: Sensitivity Analysis: Cost per capita with varied coverage rates and drug prices

	Cost per capita					
	25% coverage		50% coverage		75% coverage	
	NPR	USD	NPR	USD	NPR	USD
Lowest drug price	42.61	$0.42	85.22	$0.84	127.83	$1.25
Mean drug price	50.62	$0.50	101.25	$ 0.99	151.87	$1.49
Highest drug price	58.03	$0.57	116.06	$1.14	174.09	$1.71

Figure 2 extrapolates the per capita cost in Table 6 into population level total annual cost. At the lowest drug cost, the program cost would decline by 1 thousand to 2 thousand USD annually depending on the coverage level. Similarly, at the highest drug cost, the program cost would increase by 1 thousand to 2 thousand USD annually. The annual cost can range from lowest 4 thousand at lowest drug price- lowest coverage scenario to 17 thousand in highest drug price-highest coverage scenario.

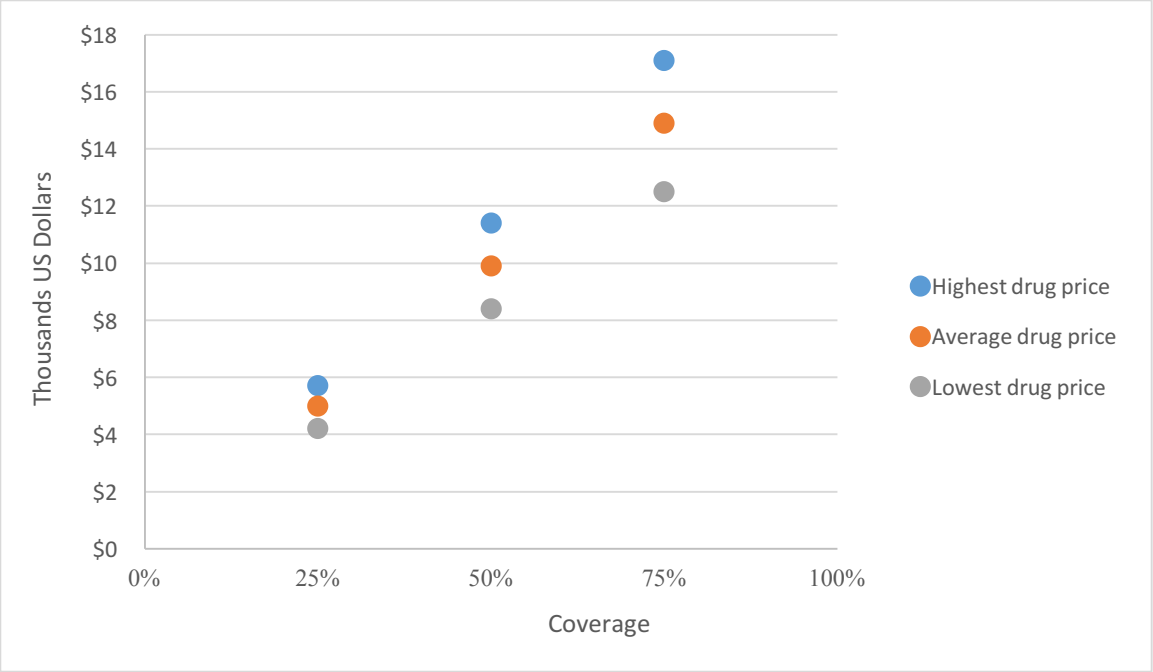

Figure 2: Annual program cost by varied coverage level and varied drug price

IV. Discussion

This study estimates the annual direct medical cost of providing risk based management of CVD according to the WHO Global HEARTS protocol in a PHCC in Nepal serving a population of 10 thousand with 50% coverage. The analysis is done from the government's perspective as it is the payer of direct health services in primary health care in Nepal. The price of laboratory analysis and human resource was based on actual costs from the Nepalese context, and the price of medicines were estimated from the MSH international drug prices using a government's purchasing rate factor. Demographic data was taken from the Nepal 2011 census, and the absolute risk profile distribution in the population was estimated from the WHO SEAR region C absolute risk profile distribution table. The comparison of cost estimates from other literatures was done by

converting the reported year USD into 2017 USD using a CPI inflation calculator from the US Bureau of Labor Statistics (https://www.bls.gov/data/inflation_calculator.htm).

Our study estimated the cost of screening eligible people to be $3 per person. This finding is similar to a WHO study which estimated the cost of screening to be $3.3 to $5.5 per person (14). While the cost of screening is inexpensive, the treatment cost per patient increases at each higher level of risk. It costs 10 times more to treat the patients with risk >30% compared to the cost of screening and managing the patients with risk <10%. This demonstrates that early screening and management can be a key strategy to prevent patients from moving into higher risk categories and incurring larger costs.

The estimated annual cost per client visiting the PHCC is $12. The estimated annual cost per capita is $1. Our result is very close to a similar study done in 2005, which estimated the cost of risk based management in low income countries to be $ 0.55 to $1.18 per capita (9). This means it will cost about $10,000 annually to a PHCC with catchment population of 10 thousand, in providing medicines, laboratory analysis and human resources for CVD prevention services to 50% of eligible population.

A cost of $1 per capita is 6.25% of the Government of Nepal's current per capita health expenditure, which is $16 (16). Regardless, the investment is justifiable because ischemic heart disease, stroke with diabetes and hypertension account for a quarter of deaths in the country (17). Although this study assumed the MoH to be the payer of health care costs, 50% of health sector budget in Nepal comes from on External Development Partners (EDPs) (18). It is likely that the cost of the program might be shared between MoH and EDPs.

The cost varies by the coverage of the service, and per capita cost is higher with higher coverage. The larger the available financial resources, the larger number of people can be reached through

the program. The total annual cost is $5,000 for 25% coverage rate, while $15,000 for 75% coverage rate. One way to reduce the cost can be to treat patients with higher risks with a pre-determined higher threshold. But, there is a tradeoff between cost and health benefits, as increasing the threshold means lower health benefits (22).

Our study estimated the direct cost of management of type 2 diabetic patients to be $38 per annum. A cross-sectional study in a public hospital in Nepal estimated the direct cost to range from $28.12 to as high as $1060.43 (23). The authors included transportation cost, food during hospital visits and in some cases also the cost of going to yoga or gym as lifestyle modification behavior. We didn't include those cost in our study. The variation in the study results might also be because we estimated the drug price with government as a payer, while the other study included both private and public facilities. The cost of cardiovascular drugs are in fact very different across different pharmacies in Nepal (24).

The cost of medicines is the largest driver of cost for each level of risk management. It is consistent with other studies which have also found the drug cost to be the highest portion of the total cost (9)(23)(19) . This means the variability in drug prices can have higher impact on variation of overall cost. The per capita cost can range from $0.8 at lowest drug price to $1.1 at highest drug price i.e. the difference of $3000 annually in total cost for a population of 10,000.

It is also important to note that the program incurs not only additional cost, but puts a demand on the existing health system as a whole. Currently PHCCs in Nepal have one physician and staff nurse employed full time, along with other paramedics. If this program is to be implemented, there is a need to add at least one-part time nurse at each facility. There is also a need to strengthen the laboratory, as this program will bring 865 people annually that need laboratory services. We

estimate that the program will also need around 300,000 units (tablet/capsule/vial) of medicines annually, which means logistic management capacity has to be increased as well.

Other studies have shown that investing in primary prevention of CVD utilizing a risk based approach is a highly cost effective intervention (9)(19)(20). Investing in primary prevention is a cost saving strategy as treating acute and post-acute IHD are more expensive than risk based management to prevent those events to occur (20). Since the Government of Nepal currently provides free heart treatment for senior citizens over 75 years, the investment in prevention today has an implication on reducing long-term expenditures for treatment of heart diseases in the elderly. Cost savings also result from reduction in mortality, as the people can remain engaged in economic activities. The expected return of investment of the intervention is very high; for every $1 spent on management of hypertension for a medium to high risk patient, there is an estimated return of investment of $23 (21).

V. CONCLUSION

For as low as $12 per case or $1 per capita in direct medical costs, primary health care centers in Nepal can provide cardiovascular prevention services. Along with the financial resources, health facilities will also need higher capacity for human resources, logistic management and laboratory services. Findings of this study can be used by program planners at the Nepalese provincial level for financial and other system resources estimation for the PHCCs for which they plan to implement the Global HEARTS program.

There are several limitations to our study. Since the program has not been currently implemented, but only planned, we heavily relied on assumptions on coverage, adherence, providers' time and drug utilization rates to develop the cost estimates. There might be variations in our resource

estimates once the program is actually being implemented. We also modelled our study with an ideal scenario where all patients are followed through our patient care pathway model. In actual practice health systems may lose some patients in each of the treatment steps from screening to treatment and follow up. We expect the price of the drugs and laboratory we used to be close approximations to actual prices, but we are also aware that this may differ from true costs. A prospective costing study during the program's actual implementation is needed to overcome these limitations. Future studies may also include other system level costs like training of human resources, logistic management, and administrative cost along with direct medical costs.

This study is one of the pioneers of costing studies in Nepal in the field of cardiovascular diseases management in PHC. The costing tool created for this study is simple and user friendly, and can be used by program planners at local level to estimate the resource need. This method of cost estimation can also be utilized in other low resource settings around the world.

REFERENCES

1. Murray CJ, Vos T, Lozano R, Naghavi M, Flaxman AD, Michaud C, et al. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. The lancet. 2013;380(9859):2197–223.

2. Global Health Estimates 2015: Estimated deaths by age, sex, and cause [Internet]. Geneva: World Health Organization, 2017; Available from: http://www.who.int/healthinfo/global_burden_disease/estimates/en/index1.html

3. Vos T, Allen C, Arora M, Barber RM, Bhutta ZA, Brown A, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. The Lancet. 2016;388(10053):1545–602.

4. Organization WH, Group IS of HW, others. Prevention of cardiovascular disease: Guidelines for assessment and management of total cardiovascular risk. WHO Geneva. 2007;

5. Global Health Estimates: Projection of deaths by cause, age and sex 2015-2030 [Internet]. World Health Organization, 2017; Available from: http://www.who.int/healthinfo/global_burden_disease/projections/en/

6. Singh GM, Danaei G, Farzadfar F, Stevens GA, Woodward M, Wormser D, et al. The age-specific quantitative effects of metabolic risk factors on cardiovascular diseases and diabetes: a pooled analysis. PloS One. 2013;8(7):e65174.

7. Global Burden of Disease Compare [Internet]. Institute of Health Metrics and Evaluation (IHME); 2017 [cited 2017 May 8]. Available from: https://vizhub.healthdata.org/gbd-compare/patterns

8. Multisectoral Action Plan on the Prevention and Control of NCD in Nepal 2014-2020. Government of Nepal;

9. Lim SS, Gaziano TA, Gakidou E, Reddy KS, Farzadfar F, Lozano R, et al. Prevention of cardiovascular disease in high-risk individuals in low-income and middle-income countries: health effects and costs. The Lancet. 2007;370(9604):2054–62.

10. National Population and Housing Census 2011. Kathmandu, Nepal: Government of Nepal, Central Bureau of Statistics; 2012 Nov. (Volume 01, NPHC 2011).

11. Noncommunicable Diseases risk factors: STEPS survey Nepal. Government of Nepal, Ministry of Health and Population; 2013.

12. WHO. HEARTS: Technical Package for cardiovascular disease management in primary health care.

13. NCD costing tool [Internet]. World Health Organization; 2012. Available from: http://www.who.int/entity/ncds/management/b_NCD_CostingTool_2012.xls?ua=1

14. WHO. Scaling up action against noncommunicable diseases: How much will it cost? World Health Organization; 2011.

15. International Medical Products Price Guide [Internet]. Management Sciences for Health (MSH); 2014 [cited 2017 Apr 10]. Available from: http://mshpriceguide.org/en/home/

16. World Health Organization. Global Health Expenditure Database [Internet]. WHO; 2014 [cited 2017 May 20]. Available from: http://apps.who.int/nha/database/Select/Indicators/en

17. GBD compare [Internet]. Seattle, US: Institute of Health Metrics and Evaluation; 2015 [cited 2017 May 23]. Available from: https://vizhub.healthdata.org/gbd-compare/

18. Sudeep Uprety, Bipul Lamichhane. Health Budgeting and Financing in Nepal: Policy Perspectives [Internet]. Health Research and Social Development forum; 2016 Aug. Available from: http://www.herd.org.np/uploads/frontend/Publications/PublicationsAttachments1/1480582316-Health Budgeting and Financing in Nepal - Policy Perspectives.pdf

19. Ha DA, Chisholm D. Cost-effectiveness analysis of interventions to prevent cardiovascular disease in Vietnam. Health Policy Plan. 2011;26(3):210–22.

20. Ortegón M, Lim S, Chisholm D, Mendis S. Cost effectiveness of strategies to combat cardiovascular disease, diabetes, and tobacco use in sub-Saharan Africa and South East Asia: mathematical modelling study. Bmj. 2012;344:e607.

21. Nugent R. Benefits and costs of the non-communicable disease targets for the post-2015 development agenda. Cph Consens Cent Perspect Pap [Internet]. 2015 [cited 2017 May 24]; Available from: https://pdfs.semanticscholar.org/1cb6/3fb64f82e3700bd85d3e688c27343f37951f.pdf

22. Murray CJ, Lauer JA, Hutubessy RC, Niessen L, Tomijima N, Rodgers A, et al. Effectiveness and costs of interventions to lower systolic blood pressure and cholesterol: a global and regional analysis on reduction of cardiovascular-disease risk. The Lancet. 2003;361(9359):717–25.

23. Shrestha N, Lohani SP, Angdembe MR, Bhattarai K, Bhattarai J, others. Cost of diabetes mellitus care among patients attending selected outpatient clinics. JNMA J Nepal Med Assoc. 2013;52:343–8.

24. Mishra SR, Kandel N, Subedi N, Khanal V. Variation in Prices of Cardiovascular Drugs in Public and Private Pharmacies in Nepal. Health Serv Res Manag Epidemiol. 2015;2:2333392814566508.