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Title: Health system and provider costs for prevention and treatment of cardiovascular and related conditions in low and middle-income countries: A systematic review

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Abstract:

Background: The burden of cardiovascular and related conditions is rapidly increasing in low- and middle-income countries, where health systems are generally ill-equipped to manage chronic disease. Policy makers and health systems need to make decisions on how to allocate limited health resources with an understanding of the drivers and costs of CVD-related conditions.

Methods: A systematic review of the published literature on providing preventive care and treatment for cardiovascular and related diseases in low- and middle-income countries was undertaken. Total costs of prevention or treatment per person or per year were inflated to 2012 USD for comparability across geographic settings and time periods.

Results: Sixty-nine articles and one hundred and eighty-five unit costs were identified regarding cardiovascular and related conditions including: treatment and prevention of CVD risks factor at the individual and population levels, treatment and prevention of ischemic heart disease, stroke, heart failure, non-ischemic heart disease, diabetes, and chronic kidney disease. Most articles evaluated clinical interventions in middle-income countries, with China, India, Brazil, and South Africa predominating. Disease prevention at the population and community levels were the lowest-cost interventions, while treatment of chronic kidney disease was the most expensive.

Conclusions: Prevention interventions and treatment of conditions at early stages are much less expensive to provide than other treatments for cardiovascular and related diseases at advanced stages. Low- and middle-income countries who are beginning to fund CVD interventions can more efficiently allocate resources given an understanding of what drives costs of CVD prevention and treatment.

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1. Introduction

1.1 Background

Cardiovascular and related diseases, such as type 2 diabetes mellitus (T2DM) and chronic kidney disease (CKD), are the leading cause of global morbidity and mortality (1). Major co-morbid conditions for cardiovascular disease, including hypertension, diabetes, and chronic kidney disease, are also increasing in prevalence, as is exposure to non-communicable disease (NCD) risk factors such as urbanization, tobacco use, and sedentary behavior (2). The growing prevalence of these conditions is particularly troublesome in low- and middle-income countries (LMICs), where age-specific rates for NCD mortality are nearly twice as high as in high-income countries(3), and treatment can be very costly for LMICs (4). There is evidence that health systems in these settings are already strained by the dual burden of infectious and chronic disease, especially in resource-limited settings (5). Many people suffering from cardiovascular disease in LMICs remain untreated, or their conditions are poorly managed, due to lack of access to primary health care and cost barriers (6).

The movement to prevent and control NCDs in LMICs is gaining momentum in the global health sector. Targets such as 25x25 and 40x30 [CITE] are unprecedented in putting NCDs on the international agenda. For these targets to become reality, however, there is a need to better understand resource utilization and the costs of treatment and prevention programs to inform their health policy and planning. Economic evaluations of cardiovascular prevention and treatment in low-resource settings are especially important for settings that do not yet have policies or the infrastructure in place to address these emerging issues (7). Unfortunately,

financial and economic cost estimates of these interventions in LMICs are limited, hindering decisions on health system planning and resource allocation.

Recent studies have examined literature on financial and economic burden or cost-effectiveness of CVD interventions in LMICs (6, 8-11). To complement this information, we present a systematic literature review of the intervention and treatment health care costs of cardiovascular and related conditions in LMICs from a provider perspective, which to date are poorly understood. We considered prevention programs and treatment costs for cardiovascular and related conditions. Specifically, we consider diabetes, chronic kidney disease, hypertension, stroke, ischemic heart disease, and non-ischemic heart diseases. We chose these conditions because of their interrelated risk factors, prevention strategies, and interventions, such as tobacco cessation or hypertension control. We will refer to the entire grouping as "CVD" throughout the remainder of the paper.

1.2 Objectives

Our primary objective is to present the level and variability in known direct medical or programmatic costs for preventing and treating CVD in LMICs. We identify gaps and suggest future economic research needs to support policy development, resource allocation, and decision making. Our secondary objective is to qualitatively assess the reasons for variations in costs across different CVD studies.

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2. Methods

2.1 Search Strategy and Article Retrieval

We conducted a disease- and country-specific systematic review of published literature following PRISMA guidelines.

The search strategy used Medline, EMBASE, NHS-EED, HEED and EconLit databases, using terms related to LMICs, economic analysis and cardiovascular disease. See Appendix 1 for the full strategy. We limited our results to articles published on or after January 1st, 2000 until approximately July 1st, 2014. In addition, we examined the references of retrieved articles and systematic reviews for potentially relevant studies. After downloading the database results, adding records from other sources and removing duplicates, researchers conducted the first round of screening by reading article titles and abstracts and discarded records that did not meet the following criteria.

- Included an economic evaluation
- Included evaluation of at least one low- or middle-income country (as defined by the World Bank)
- Referred to our previously standardized list of cardiovascular or related-related conditions
- Made available in English
- Published on or after January 2000.

Two independent reviewers screened the full text of the remaining articles. We used both the Drummond Checklist and Mogyorosy and Smith's 2012 literature review for guidance in creating the following guidelines regarding quality and inclusion[12, 13]:

- The study must have conducted at least one type of economic evaluation, including cost analysis, cost-effective analysis, or cost-utility analysis, with clearly presented unit cost data.
- We did not consider studies with net costs presented only in ratios, such as disabilityadjusted life years (DALYs), quality adjusted life years (QALYs), or life-years saved (LYS).
- The paper must have utilized either original unit cost data regarding a CVD intervention, or unit costs from a credible and known source, such as WHO-CHOICE.
- The paper must have presented direct intervention costs (medical or programmatic) from the provider perspective, regardless of payer or indirect costs. Studies from alternative perspectives were considered if they delineated provider costs.
- The study had to meet certain quality standards, which includes having a description of the intervention and analysis, detailing the time and location of data collection, and clearly stating the year and currency of presented costs (See Figure 1 for Article Selection Process).

2.2 Data Extraction

We created an excel database and entered detailed information on each eligible study, including condition, country or region, target population, type of treatment or intervention, and level of care. We also noted study methods, such as: type of economic evaluation, perspective, sample size, exchange rate, discount rate, sensitivity analysis, and cost categories and metrics. The total treatment or intervention costs, defined as the total cost per patient, per beneficiary, or per capita, were extracted in their original currency and year. For acute events, we used the total cost per patient as presented. For recurring costs, such as hemodialysis treatments or ongoing hypertension management, we pulled the cost per treatment or per year. Inpatient or outpatient visit data were noted where available. Most studies included multiple data points, particularly if they discussed more than one CVD intervention or more than one geographic setting.

We converted all costs to US Dollars (2012), the currency and year in which we present all costs in this paper. When possible, we extracted the data in local currency units (LCUs), inflated it to

2012 rates using the World Bank consumer price indices, and converted it to 2012 US Dollars via World Bank rates. When costs were presented for regions, we used the largest LMIC country in the region as a proxy. For data presented in international dollars, we converted it back into LCUs using World Bank Purchasing Power Parity, then followed our standard processes. Once the data was in a common currency, we grouped similar interventions and qualitatively compared the magnitudes and variability of total and input costs. We combined data into two overarching groups: risk factor (prevention) and disease (treatment) interventions. The first group was further broken down into individual-level and population-level interventions for risk factors. The treatment group focused specifically on ischemic heart disease, non-ischemic heart diseases, stroke, heart failure, type two diabetes mellitus, and chronic kidney disease.

3. Results

The systematic search identified 3809 unique articles, of which 181 were retrieved for full-text review. 69 studies met our final inclusion criteria, presenting approximately 185 unit costs (See Figure 1: Article Selection Flow Chart). The majority of articles were excluded after the initial screening because they were duplicates or they clearly did not meet basic inclusion criteria.

3.1 Basic characteristics of studies

The number of published articles for CVD costs in LMICs has increased dramatically since 2000, as seen in Figure 2. In fact, we identified only five articles in the years 2000-2006, increasing to 16 articles published in 2013 alone. Most of the cost data reflected clinical treatments in urban areas of middle income countries, with less than half of the studies assessing costs at a rural, regional, or national level (n=30).

The cost data was concentrated in Asian countries (n=41), primarily driven by India (n=10) and China (n=14). In fact, over a quarter of our cost data came from China; India contributed the next highest amount of data at 12%. One-third of our cost data concerned diabetes, which was a considerably higher proportion than any other condition, and two-thirds of those diabetes costs were from Asian-based studies. Sub-Saharan Africa, by contrast, mainly produced data regarding stroke and hypertension. Other regions did not produce noteworthy cost trends by condition.

Although most of the interventions took place in traditional healthcare settings, we identified policy and platform costs as well. Six studies (n=6) produced 18 data points regarding policy costs, mainly concerning diabetes awareness, salt reduction, and tobacco regulation. Ten studies (n=10) looked at interventions conducted from non-clinical platforms, including schools, community centers, and home-health programs. One study even looked at shutting down main streets periodically to promote physical activity.

3.2 Economic evaluation methods

We obtained cost data from a variety of economic evaluations. More than half of the articles (n=39) were cost analyses, meaning they only collected and presented data on costs, although many cost-effectiveness analyses and cost-of-illness studies, which collect and present other data in addition to costs, met our inclusion criteria as well (n=24, n=6 respectively). More studies were empirical than modeled (n=51, n=28 respectively), with data from an actual event rather than making predictions about hypothetical events. In the empirical studies, most of the data was

collected retrospectively (n=29) by reviewing health records (n=33). The 17 remaining studies used an ingredients approach, taking the sum cost of activities and resources used, and only one study used a questionnaire to collect data. Of the 69 studies, about half converted their costs in US Dollars for presentation (n=35). Although it is difficult to measure the quality of a study objectively, economic evaluation guidelines recommend discounting future costs and conducting sensitivity analyses when assumptions are made. We noted that approximately one-third of the studies conducted sensitivity analysis, and one-third used discounting in their methods; 15 articles used both.

The majority of studies were from a provider perspective (n=39), however we also included 31 studies using either societal or patient perspective (n=22, n=9 respectively). The latter types of studies were included because they disaggregated the direct medical costs from other costs, including out-of-pocket expenses, transportation, and foregone income. About one-half of the studies disaggregated their costs into categories, the most common of which were personnel, diagnostic tests, screening, medications, and hospitalization fees. Papers with disaggregated cost inputs were more likely to mention cost aspects of condition severity, length of inpatient stay, and the influence of medical complications. These are important factors in understanding what drives the cost of CVD care, and allowed for a degree of comparison.

3.3 Population level costs for the prevention of cardiovascular disease, diabetes & kidney disease

Many of the World Health Organization's (WHO) designated best buys for CVD prevention occur at a population level, seeking to affect environmental elements and bypassing common barriers to healthcare access. Unfortunately, information on the costs of enacting populationlevel interventions was limited relative to costs for person-directed or clinical interventions. Of ten articles identified, four addressed tobacco reduction(14-17), three presented legislation or policies to reduce salt intake(14, 17, 18), three articles regarding diabetes prevention (18-21), and three articles that addressed health promotion in the general population(14, 22, 23). We did not identify population-level prevention costs from any low-income countries, or any place located in sub-Saharan Africa. Tobacco taxation, one of the most cost-effective tools to prevent CVD, was generally outside the scope of our study given the complex nature of tax structures.

The average cost of national prevention programs ranged from less than $0.01 to $2.84 per capita. Low per capita costs can quickly translate into high overall program costs depending on the country's population and geographic distribution to reach at risk or hard to reach populations. Three studies mentioned diabetes prevention costs, engaging tactics such as mass media campaigns, nationwide screening programs, and community health promotion programs, for which media campaigns were by far the cheapest (19-21). Total program costs varied from $11,000 per year to implement graphic warning labels on cigarette packaging in Vietnam to more than $200 million per year to enforce processed foods salt reduction in Turkey (16, 18). Two papers used school as platforms to reach individual children. The program for tobacco cessation

education cost about $13,000 per school for a two year program; the childhood obesity reduction combined various nutrition and physical activity interventions to cost between $9-$31 per participant (15, 22). Whether at the national, community, or school level, population-level interventions aimed at behavior modification and awareness were relatively inexpensive.

3.4 Individual level costs for the prevention of cardiovascular disease, diabetes & kidney disease

CVD prevention on an individual level, including regular medical checkups, screenings, and preventive medication, require a certain level of healthcare infrastructure. This may explain why we did not identify any individual prevention costs for low-income countries or countries in subSaharan Africa. We identified nine articles with individual prevention costs, although due to the interrelated nature of CVD conditions, many treatments covered in the following sections may be considered prevention for other conditions. Primary prevention of CVD took place in either community health centers or with home health education, costing about $5 in Pakistan and $8 in China (24, 25). Screening for dyslipidemia in Thailand cost around $5 per screening and $37 per case detected (26, 27). Bupropion treatment for tobacco cessation cost about $123 per patient per year in Argentina (28). Prevention of rheumatic heart disease cost $26-$46 in India, depending on the level of care. Salomon et al (2012) calculated the national cost for individual prevention of stroke, heart failure and T2DM, which cost roughly $0.16, $0.03, and $0.53 per capita per year respectively(17).

3.5 Individual level costs for treating ischemic heart disease (IHD)

Ischemic heart disease (IHD) treatment costs generally correlated with levels of severity, from outpatient treatment of hypertension to hospitalization for severe acute events, such as a heart

attack. Hypertension treatment with outpatient visits and medication cost about $40 per patient per year in both Tanzania and Thailand(29, 30). One paper totaled the annual cost of hypertension management at $169 in South Africa, although the components of this total are unclear(31). The annual cost of managing hypertension in China, including inpatient and outpatient care as well as medication, cost about $566 per patient per year according to one study. Another study based in China reported that an inpatient visit averaged $817 and an outpatient visit averaged $20 (32, 33). Three studies focused on pharmacological treatment, which varied by location and type of medication. In Argentina, annual medication for high blood pressure and high cholesterol cost $52 and $125 respectively, with the modified polypill strategy costing about $109 annually(28). Hypertension drug costs varied in sub-Saharan Africa, ranging from $2-$17 in Nigeria, and $2-$76 in Tanzania(34, 35). Both papers noted that advanced hypertension and the need to take several medications simultaneously drove the higher end of the range.

Beyond hypertension management, treatment of IHD typically consists of diagnostic procedures (36), surgical procedures (31, 36-38), and post-operative care (31, 39). An inpatient visit averaged $8,800, with a range from $2,304 to $22,500. The highest inpatient costs were associated with longer hospitalization periods, more severe conditions, and surgical interventions (28, 33, 40). The costs of surgical procedures, including catheter-based procedures (stenting and angioplasty) or coronary artery bypass surgery (CABG), ranged from $4,000-$22,000 per patient per procedure depending on the diagnostics, the complexity of the procedure, and whether medical therapy and recovery costs are included in the total cost estimates. A CABG procedure

cost $10,000 in China and $22,000 in South Africa, although both costs were pulled from hospital price lists and were not itemized (31, 36). Gaziano et al (31) noted in their model that preventative treatment of IHD, based on absolute risk rather than on target blood pressure, was important due mainly to high costs of surgery and post-operative care. Surgical interventions also carry a risk of hospital-acquired infections which substantially raises the cost of an IHD procedure; one study in India estimated bacteremia caused the cost to increase by as much as $21,000 (39). Of the five papers identified with costs of IHD surgical procedures, only one broke down that cost into sub-categories that included bed charges, diagnostics, medication, consultation, surgery, blood bank, and bedside procedures (31, 36-39). The others simply cited private hospital data for their unit costs. Information on surgical procedure costs comes mainly from middle income countries, with very little information from low income countries.

3.6 Individual level costs for treating stroke

We identified 16 articles analyzing stroke care in LMICs, which is a large amount of robust data relative to available data for other conditions. Our search returned data on two types of stroke: ischemic stroke, which occurs as a result of an obstruction in a blood vessel to the brain, and hemorrhagic stroke, which occurs when a blood vessel ruptures in the brain. Ischemic stroke is the more common of the two, is generally easier to treat, and has a lower case-fatality rate. These characteristics often lead to lower treatment costs. Four articles compared the costs of hemorrhagic stroke (HS) and ischemic stroke (IS) treatment (41-44). In Turkey and Brazil, the mean provider cost of treating HS were approximately 50% higher than IS (41, 42). This trend held true to a lesser extent in Chinese study, where HS cost about 19% more than IS care; the difference between subtypes in Malaysia was not significant (43, 44). In all four articles, the

subtypes of stroke had similar imaging and lab work costs, however hemorrhagic strokes were generally more severe, required longer hospital stays, and involved surgical or intensive care unit costs.

The majority of articles provided the inpatient cost per stroke event, but did not distinguish the type of strokes (28, 31, 43-48). Differences in inpatient costs reflected variation in geographic setting, clinical capacity, and average length of stay. In Congo, a low-income countries, the average length of stay was less than 6 days and the average cost was $400 per inpatient stay (45). In Pakistan, another low-middle income country, average inpatient costs with mean LOS 3-5 days varied by ward type, ranging in cost from $1800 in the general ward to $6500 in the intensive care unit (49). In China and Malaysia, inpatient care costs ranged from $1140 to $2407 depending on the LOS, which averaged 6.5 days in Malaysia and was as high as 20 days in China (43, 44, 47, 48). Inpatient costs for treating stroke were higher in upper income countries, with $3630 per inpatient stay in Argentina and about $17000 in South Africa. A single paper looked at identifying patients at high-risk for stroke in order to provide preventive care in China; these interventions, including medication, behavior modification, in- and out-patient visits, cost about $500 per year (48).

3.7 Population and individual level costs for treating type 2 diabetes mellitus (T2DM) and chronic kidney disease (CKD)

Type 2 diabetes mellitus management focuses on many of the same behavior changes as CVD, and if neglected can lead to complications such as ulcers, blindness, and kidney failure. Diabetic foot ulcers and retinopathy were the most cited consequences of untreated diabetes, with severity

and screening driving the costs of both (50-54). T2DM treatment costs in LMICs varied significantly due to ranging severities, comorbidities and sequelae. Inpatient costs are available only from middle-income countries supplied (33, 55-58); outpatient costs ranged from $5 per visit in Thailand to $34 in China (33, 55, 59, 60). Seven articles discussed annual care costs to manage T2DM in a clinic or community health center setting, costing on average $400 ($77$1,336). The average to manage diabetes in a hospital setting rose to $990 ($56-$2,480) per year (56, 61-66). Screening and diagnostic costs varied from population-wide programs to community screening programs.

Chronic kidney disease treatment, including that of end-stage renal disease (ESRD), consisted of long-term dialysis and renal transplant costs. One session of hemodialysis for ESRD could cost $79 in Jordan, $80 in Sudan and $97 in Iran (65, 67, 68). ESRD treatment in China, Malaysia, and Thailand varied from $29,000 to $106,000, including dialysis, renal transplants, and postoperative maintenance (69). Kidney transplantation and post-operative maintenance for kidney failure ran from $5,000 to $21,000 in the Sudan and Iran, respectively (68, 70).

3.8 Individual level costs for treating heart failure and non-ischemic heart diseases

Other types of heart conditions, such as heart failure, Chagas cardiomyopathy (CC), congenital heart disease, and rheumatic heart disease, are important sources of health burden in LMICs, however the literature on their treatment costs is sparse. Treatment costs of heart failure were poorly described and difficult to compare across settings, although CC was found to be more expensive to treat than heart failure from other etiologies (71). Other literature focused on preventing and treating rheumatic fever to avoid high costs of rheumatic heart disease treatment

(72-74). One paper based in a tertiary hospital in Brazil noted that congenital heart surgery and post-operative care would cost around $1,500 per patient.

4. Discussion

This study highlights the paucity of quality cost data on cardiovascular and related diseases in LMICs and underscores the need for caution when interpreting cost data from multiple studies. The available data reveals that treatment of advanced cardiovascular and related diseases is prohibitively expensive for most people living in LMICs, and little is known about the costs of scaling up prevention and early treatment interventions to avoid catastrophic health expenditures. Focusing on what is known about CVD costs, we urge future studies to disaggregate their cost inputs for more robust interpretation of results and we highlight particular areas for further economic exploration.

4.1 The complexity and variation in cardiovascular and related condition costs

Treating CVD and its risk factors is complex, due in part to the interrelationship between hypertension, diabetes, and ischemic heart disease, and the fact that multiple shared risk factors affect CVD health outcomes. The clinical heterogeneity of CVD can make treatment costs for a single condition much more variable than in the case of infectious diseases or some other chronic diseases. For instance, CVD encompasses different types of heart and related diseases, such as hypertension, stroke, and heart failure, with different levels of severity, and associated care and management. There are numerous clinical protocols for treating complicated conditions, and treatment includes different combinations of drugs, diagnostics and imaging technologies, surgery and different requirements for inpatient care and follow-up visits, making comparisons

between studies all but impossible. Additionally, there are large variations in clinical characteristics, capabilities, and practices among and within countries; it is possible to have a wide distribution of costs even within a hospital if they offer various levels of care, such as general, specialty, and intensive care wards(49).

The variation in cost methodology in our identified body of literature is one reason for the observed variation in costs. There was a lack of standard reporting across the studies, most notably in the failure to describe cost ingredients. When studies disaggregated costs, there were not clear and common categories for input or activity cost categories. In addition, for disaggregated input costs, it was unclear when activities included personnel in the costs. Many studies provided costs for imaging, diagnostic or therapeutic services, without indicating whether personnel costs were included. Surgery was a common category, but descriptions of what resources comprised surgery or surgical procedures were absent from the majority of the studies. We also noticed a lack of clinical protocol reporting in publications. Using established and accepted protocols for CVD interventions to guide economic evaluations has the potential to increase comparability across studies and accessibility for clinicians.

Trends in the data emerged despite these limitations. Cost data was most informative when disaggregated into categories and inputs, allowing the reader to better understand heterogeneity and make more useful comparisons. Empirical and modeling studies were both beneficial, however the empirical studies presented more detailed data based on inputs and the main drivers

of costs. Modeling studies were often vague about their cost inputs, but were able to capture longer time frames and larger populations, which are important aspects for policy-makers to consider.

Promotion and primary prevention were less expensive and had lower unit costs than treating CVD, and this finding is consistent for each condition where data is available, including heart disease, stroke, and diabetes. The least expensive intervention were population prevention strategies to reduce tobacco use and salt consumption, both listed as WHO Best Buys, while chronic kidney disease was the most expensive to treat of all conditions followed by surgical interventions for ischemic heart disease (Figure 3). Promotion policies for salt, tobacco and cholesterol control were inexpensive at less than $1.00 per person per year, but also ranged from around $0.15 per person per year for mass media campaigns to a higher average cost of $0.80 per person per year for cholesterol control (14). Tobacco cessation programs costs vary and depend on whether individual or population based platforms are being used. For example, average unit costs ranged from less than a cent per person per year for package warnings in Vietnam (Solomon 2012) to $10,000 for school based smoking cessation programs in India (15). These cost estimates are useful for considering scaling up national prevention programs, as low per capita costs can quickly translate into high overall program costs depending on the country's population and geographic distribution.

4.2 Gaps in the literature

Our review identified critical gaps in information and demonstrated substantial heterogeneity in both prevention and treatment costs for CVD across the limited available data for LMIC

countries. The most obvious gap was the need for more consistent methodology, with clear presentation of data on cost ingredients and drivers. Cost data is used to inform resource allocation and to improve efficiency; health policy officials need to understand the underlying causes of health expenditures in order to make nuanced decisions. We identified no longitudinal studies in LMICs, however several modelled studies looked at health costs over a longer period of time. Longitudinal studies would be particularly revealing regarding costs of chronic conditions, such as hypertension and diabetes, which require lifelong management. In the absence of longitudinal studies, health decision-makers are allocating CVD resources with an incomplete picture of future costs.

There have been very few economic evaluations of CVD conditions conducted in low-income countries. While these countries are likely the most heavily resource-constrained, they are also likely the least prepared to prevent and treat CVD conditions. Particularly distressing is the fact that we found no data on the cost of diabetes care in low-income countries. Middle-income countries, particularly upper-middle income countries such as Brazil, China, and South Africa, have produced research or publications regarding technologically-complex interventions, revealing relatively higher health system capacity. As the double-burden of infectious and chronic conditions increases, and policy makers in low-income countries divert health resources to the chronic conditions, published studies from other LMICs can provide economic evidence on CVD interventions. Population-level interventions will be important, as tobacco cessation, salt reduction, and physical activity promotion are inexpensive policies that can prevent a large portion of CVD burden. Platforms to reach low-resource populations will also be important study

subjects, as schools, mobile clinics, community programs, peer-education programs, and primary care facilities will be the best outlets for prevention and early management of CVD conditions.

5. Conclusion

Settings that do not currently offer NCD services will be looking for relevant costing data and information to use for guidance in their national planning. The current body of available literature underscores common sense regarding chronic disease: prevention is cheaper than treatment, and management of conditions is cheaper in early stages rather than advanced. Primary prevention and early management care can occur at primary care levels with less sophisticated human resource and equipment needs, making local health delivery platforms an attractive option in low-resource settings. There is currently a sub-optimal amount of evidence for CVD treatment and prevention costs in LMICs, particularly low-income countries.

As NCD prevalence grows, there will certainly be more research on the cost of implementing CVD interventions in low-resource settings. To inform the design, implementation, and scale-up of evidence-based interventions, there will be demand for high quality cost data. Such data will be critical inputs into decision makers' assessment for investing in the reduction of NCDs, such as CVD. In addition to following recommended costing analysis protocol, future research on the costs of CVD prevention and care should prioritize understanding cost drivers in interventions to inform resource-constrained health policy. Standard methods of care or clinical protocol should be used to inform costing studies when possible. Future research should either use these protocols to conduct economic analyses, or at least as a reference point, to make cost studies more comparable and highlight differences in available treatment across settings.

Global prevalence of cardiovascular and related conditions will continue to increase in the absence of aggressive interventions. Aware of the risks, costs, and available interventions, decision-makers' best option is to act early in order to reduce and prevent the harm these conditions cause on individuals and communities.

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7. References

1. Murray CJ, Vos T, Lozano R, al. e. 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. Lancet. 2012;380(9859):2197-223.
2. Lim S, Vos T, Flaxman A, al. e. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. . Lancet. 2012;380(9859):2224-60.
3. Organization WH. Preventing chronic diseases: a vital investment: World Health Organization; 2005.
4. Yusuf S, Rangarajan S, Teo K, Islam S, Li W, Liu L, et al. Cardiovascular Risk and Events in 17 Low-, Middle-, and High-Income Countries. New England Journal of Medicine. 2014;371(9):818-27.
5. Jamison DT, Summers LH, Alleyne G, Arrow KJ, Berkley S, Binagwaho A, et al. Global health 2035: a world converging within a generation. The Lancet. 2013;382(9908):1898955.
6. Kankeu HT, Saksena P, Xu K, Evans DB. The financial burden from non-communicable diseases in low- and middle-income countries: a literature review. Health research policy and systems / BioMed Central 2013;11(31).

7. Suhrcke M, Boluarte TA, Niessen L. A systematic review of economic evaluations of interventions to tackle cardiovascular disease in low- and middle-income countries. BMC public health. 2012;12:2.
8. Asaria P, Fortunato L, Fecht D, Tzoulaki I, Abellan JJ, Hambly P, et al. Trends and inequalities in cardiovascular disease mortality across 7932 English electoral wards, 1982–2006: Bayesian spatial analysis. International journal of epidemiology. 2012;41(6):1737-49.
9. Jamison DT, Breman JG, Measham AR, Alleyne G, Claeson M, Evans DB, et al. Disease control priorities in developing countries: World Bank Publications; 2006.
10. Samb B, Desai N, Nishtar S, Mendis S, Bekedam H, Wright A, et al. Prevention and management of chronic disease: a litmus test for health-systems strengthening in lowincome and middle-income countries. The Lancet. 2010;376(9754):1785-97.
11. Alam K, Mahal A. Economic impacts of health shocks on households in low and middle income countries: a review of the literature. Globalization and health. 2014;10(1):21.
12. Drummond M, Jefferson T. Guidelines for authors and peer reviewers of economic submissions to the BMJ. The BMJ Economic Evaluation Working Party. BMJ: British Medical Journal. 1996;313(7052):275.
13. Mogyorosy Z, Smith P. The main methodological issues in costing health care services: a literature review. 2005.
14. Ha DA, Chisholm D. Cost-effectiveness analysis of interventions to prevent cardiovascular disease in Vietnam. Health policy and planning. 2011;26(3):210-22.
15. Brown HS, 3rd, Stigler M, Perry C, Dhavan P, Arora M, Reddy KS. The cost-effectiveness of a school-based smoking prevention program in India. Health Promot Int. 2013;28(2):17886.
16. Higashi H, Truong K, Barendregt JJ, Nguyen PK, Vuong ML, Nguyen TT, et al. Cost Effectiveness of Tobacco Control Policies in Vietnam: The Case of Population-Level Interventions. Journal of Applied Health Economics and Health Policy. 2011;9(3):183-96.
17. Salomon JA, Carvalho N, Gutierrez-Delgado C, Orozco R, Mancuso A, Hogan DR, et al. Intervention strategies to reduce the burden of non-communicable diseases in Mexico: cost effectiveness analysis. Bmj. 2012;344:e355.
18. Mason H, Shoaibi A, Ghandour R, O'Flaherty M, Capewell S, Khatib R, et al. A Cost Effectiveness Analysis of Salt Reduction Policies to Reduce Coronary Heart Disease in Four Eastern Mediterranean Countries. PloS one. 2014;9(1):e84445.
19. Liu X, Li C, Gong H, Cui Z, Fan L, Yu W, et al. An economic evaluation for prevention of diabetes mellitus in a developing country: a modelling study. BMC public health. 2013;13(1):1-11.
20. Toscano CM, Duncan BB, Mengue SS, Polanczyk CA, Nucci LB, Costa e Forti A, et al. Initial impact and cost of a nationwide population screening campaign for diabetes in Brazil: a follow up study. BMC Health Serv Res. 2008;8:189.
21. Zhang YL, Gao WG, Pang ZC, Sun JP, Wang SJ, Ning F, et al. Diabetes self-risk assessment questionnaires coupled with a multimedia health promotion campaign are cheap and

effective tools to increase public awareness of diabetes in a large Chinese population. Diabet Med. 2012;29(11):e425-9.
22. Meng L, Xu H, Liu A, van Raaij J, Bemelmans W, Hu X, et al. The costs and costeffectiveness of a school-based comprehensive intervention study on childhood obesity in China. PloS one. 2013;8(10):e77971.
23. Montes F, Sarmiento OL, Zarama R, Pratt M, Wang G, Jacoby E, et al. Do health benefits outweigh the costs of mass recreational programs? An economic analysis of four Ciclovia programs. J Urban Health. 2012;89(1):153-70.
24. Jafar TH, Islam M, Bux R, Poulter N, Hatcher J, Chaturvedi N, et al. Cost-effectiveness of community-based strategies for blood pressure control in a low-income developing country: findings from a cluster-randomized, factorial-controlled trial. Circulation. 2011;124(15):1615-25.
25. Bai Y, Zhao Y, Wang G, Wang H, Liu K, Zhao W. Cost-effectiveness of a hypertension control intervention in three community health centers in China. J Prim Care Community Health. 2013;4(3):195-201.
26. Sanguantrakul U, Jiamjarasrangsi W, Vimolket T. Efficiency and cost-effectiveness of dyslipidemia screening methods among workers in Bangkok. Southeast Asian Journal of Tropical Medicine and Public Health. 2010;41(1):215.
27. Wiroj Jiamjarasrangsi M, Wichai Aekplakorn M. Cost and effectiveness of screening methods for abnormal fasting plasma glucose among Thai adults participating in the annual health check-up at King Chulalongkorn Memorial Hospital. J Med Assoc Thai. 2011;94(7):833-41.
28. Rubinstein A, Colantonio L, Bardach A, Caporale J, Marti SG, Kopitowski K, et al. Estimation of the burden of cardiovascular disease attributable to modifiable risk factors and cost-effectiveness analysis of preventative interventions to reduce this burden in Argentina. BMC public health. 2010;10:627.
29. Ngalesoni F, Ruhago G, Norheim OF, Robberstad B. Economic cost of primary prevention of cardiovascular diseases in Tanzania. Health policy and planning. 2014.
30. Pannarunothai S, Kongpan M, Mangklasiri R. Costs-effectiveness of the urban health center in Nakhon Ratchasima: a case study on diabetes and hypertension. Journal of the Medical Association of Thailand= Chotmaihet thangphaet. 2001;84(8):1204-11.
31. Gaziano TA, Steyn K, Cohen DJ, Weinstein MC, Opie LH. Cost-effectiveness analysis of hypertension guidelines in South Africa: absolute risk versus blood pressure level. Circulation. 2005;112(23):3569-76.
32. Le C, Zhankun S, Jun D, Keying Z. The economic burden of hypertension in rural southwest China. Trop Med Int Health. 2012;17(12):1544-51.
33. Zhao W, Zhai Y, Hu J, Wang J, Yang Z, Kong L, et al. Economic burden of obesity-related chronic diseases in Mainland China. Obesity Reviews: International Association for the Study of Obesity. 2007;9(Suppl. 1):62-7.

34. Robberstad B, Hemed Y, Norheim OF. Cost-effectiveness of medical interventions to prevent cardiovascular disease in a sub-Saharan African country--the case of Tanzania. Cost Eff Resour Alloc. 2007;5:3.
35. Ilesanmi OS, Ige OK, Adebiyi AO. The managed hypertensive: the costs of blood pressure control in a Nigerian town. The Pan African medical journal. 2012;12(101517926):96.
36. Cheng MM, Lu B, Hu SS, Marelli C, Higashi MK, Patel PA, et al. Optimizing CAD diagnosis in China with CT angiography. J Cardiovasc Comput Tomogr. 2009;3(3):153-8.
37. Fernandes A, Mansur AJ, Canêo LF, Lourenço DD, Piccioni MA, Franchi SM, et al. The Reduction in Hospital Stay and Costs in the Care of Patients with Congenital Heart Diseases Undergoing Fast-Track Cardiac Surgery. Arquivos Brasileiros de Cardiologia. 2004;83(1).
38. Perikhanyan A. Effectiveness and cost-effectiveness of coronary artery bypass surgery versus drug eluting stents in armenia: a feasibility study. Georgian Medical News. 2011;6(195).
39. Kothari A, Sagar V, Ahluwalia V, Pillai BS, Madan M. Costs associated with hospitalacquired bacteraemia in an Indian hospital: a case-control study. J Hosp Infect. 2009;71(2):143-8.
40. Ross H, Trung DV, Phu VX. The costs of smoking in Vietnam: the case of inpatient care. Tob Control. 2007;16(6):405-9.
41. Asil T, Celik Y, Sut N, Celik AD, Balci K, Yilmaz A, et al. Cost of acute ischemic and hemorrhagic stroke in Turkey. Clinical neurology and neurosurgery. 2011;113(2):111-4.
42. Christensen MC, Valiente R, Sampaio Silva G, Lee WC, Dutcher S, Guimaraes Rocha MS, et al. Acute treatment costs of stroke in Brazil. Neuroepidemiology. 2009;32(2):142-9.
43. Nordin N, Aljunid S, Aziz N, Nur AM, Sulong S. Direct Medical Cost of Stroke: Findings from a Tertiary Hospital in Malaysia. Medical Journal of Malaysia. 2012;67(5).
44. Wei JW, Heeley EL, Jan S, Huang Y, Huang Q, Wang JG, et al. Variations and determinants of hospital costs for acute stroke in China. PLoS One. 2010;5(9).
45. Gombet TR, Ellenga-Mbolla BF, Ikama MS, Ekoba J, Kimbally-Kaky G. Coût financier de la prise en charge des urgences cardiovasculaires au Centre Hospitalier et Universitaire de Brazzaville. Médecine Tropicale. 2009;69:45-7.
46. Khealani BA, Javed ZF, Syed NA, Shafqat S, Wasay M. Cost of acute stroke care at a tertiary care hospital in Karachi, Pakistan. JPMA The Journal of the Pakistan Medical Association. 2003;53(11):552-5.
47. Ma Y, Liu Y, Fu HM, Wang XM, Wu BH, Wang SX, et al. Evaluation of admission characteristics, hospital length of stay and costs for cerebral infarction in a medium-sized city in China. Eur J Neurol. 2010;17(10):1270-6.
48. Zhao JJ, He GQ, Gong SY, He L. Status and costs of primary prevention for ischemic stroke in China. J Clin Neurosci. 2013;20(10):1427-32.
49. Khealani B, Javed ZF, Syed N, Shafqat S, Wasay M. Cost of Acute Stroke Care at a tertiary care hospital in Karachi, Pakistan. Journal of Pakistani Medical Association. 2003;53(11).

50. Ali SM, Fareed A, Humail SM, Basit A, Ahmedani MY, Fawwad A, et al. The personal cost of diabetic foot disease in the developing world--a study from Pakistan. Diabet Med. 2008;25(10):1231-3.
51. Cavanagh P, Attinger C, Abbas Z, Bal A, Rojas N, Xu Z-R. Cost of treating diabetic foot ulcers in five different countries. Diabetes/metabolism research and reviews. 2012;28 Suppl 1(dcy, 100883450):107-11.
52. Ogbera AO, Fasanmade O, Ohwovoriole AE, Adediran O. An assessment of the disease burden of foot ulcers in patients with diabetes mellitus attending a teaching hospital in Lagos, Nigeria. Int J Low Extrem Wounds. 2006;5(4):244-9.
53. Khan T, Bertram MY, Jina R, Mash B, Levitt N, Hofman K. Preventing diabetes blindness: cost effectiveness of a screening programme using digital non-mydriatic fundus photography for diabetic retinopathy in a primary health care setting in South Africa. Diabetes research and clinical practice. 2013;101(2):170-6.
54. Rachapelle S, Legood R, Alavi Y, Lindfield R, Sharma T, Kuper H, et al. The cost-utility of telemedicine to screen for diabetic retinopathy in India. Ophthalmology. 2013;120(3):566-73.
55. Chatterjee S, Riewpaiboon A, Piyauthakit P, Riewpaiboon W, Boupaijit K, Panpuwong N, et al. Cost of diabetes and its complications in Thailand: a complete picture of economic burden. Health & social care in the community. 2011;19(3):289-98.
56. Cobas RA, Ferraz MB, Matheus AS, Tannus LR, Negrato CA, Antonio de Araujo L, et al. The cost of type 1 diabetes: a nationwide multicentre study in Brazil. Bull World Health Organ. 2013;91(6):434-40.
57. Kumpatla S, Kothandan H, Tharkar S, Viswanathan V. The Costs of Treating Long Term Diabetic Complications in a Developing Country: A Study from India. Journal of the Association of Physicians India. 2013;61.
58. Tharkar S, Satyavani K, Viswanathan V. Cost of medical care among type 2 diabetic patients with a co-morbid condition--hypertension in India. Diabetes research and clinical practice. 2009;83(2):263-7.
59. Shrestha N, Lohani S, Angdembe M, Bhattarai K, Bhattarai J. Cost of Diabetes Mellitus Care among Patients attending selected Outpatient Clinics. Journal of Nepal Medical Association. 2013;52(190):343-8.
60. Khowaja LA, Khuwaja AK, Cosgrove P. Cost of diabetes care in out-patient clinics of Karachi, Pakistan. BMC health services research. 2007;7(101088677):189.
61. Li H, Chen BK, Shah N, Wang Z, Eggleston KN. Socioeconomic correlates of inpatient spending for patients with type 2 diabetes mellitus in China: evidence from Hangzhou. Exp Clin Endocrinol Diabetes. 2012;120(1):35-44.
62. Ramachandran A, Snehalatha C, Yamuna A, Mary S, Ping Z. Cost-Effectiveness of the Interventions in the Primary Prevention of Diabetes Among Asian Indians. Diabetes Care. 2007;30(10).

63. Wang W, Fu CW, Pan CY, Chen W, Zhan S, Luan R, et al. How Do Type 2 Diabetes MellitusRelated Chronic Complications Impact Direct Medical Cost in Four Major Cities of Urban China. Value Health. 2009;12(6):923-9.
64. Akari S, Mateti UV, Kunduru BR. Health-care cost of diabetes in South India: A cost of illness study. Journal of research in pharmacy practice. 2013;2(3):114-7.
65. Arefzadeh A, Lessanpezeshki M, Seifi S. The cost of hemodialysis in Iran. Saudi journal of kidney diseases and transplantation : an official publication of the Saudi Center for Organ Transplantation, Saudi Arabia. 2009;20(2):307-11.
66. Riewpaiboon A, Pornlertwadee P, Pongsawat K. Diabetes cost model of a hospital in Thailand. Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research. 2007;10(4):223-30.
67. Al-Shdaifat EA, Manaf MR. The economic burden of hemodialysis in Jordan. Indian J Med Sci. 2013;67(5-6):103-16.
68. Elsharif ME, Elsharif EG, Gadour WH. Costs of hemodialysis and kidney transplantation in Sudan: a single center experience. Iranian journal of kidney diseases. 2010;4(4):282-4.
69. Annemans L, Demarteau N, Hu SS, Lee T, Morad Z, Supaporn T, et al. An Asian Regional Analysis of Cost-Effectiveness of Early Irbesartan Treatment versus Conventional Antihypertensive, Late Amlodipine, and Late Irbesartan Treatments in Patients with Type 2 Diabetes, Hypertension, and Nephropathy. Value In Health. 2008;11(3):354-64.
70. Nourbala MH, Einollahi B, Kardavani B, Khoddami-Vishte HR, Assari S, Mahdavi-Mazdeh M, et al. The cost of kidney transplantation in Iran. Transplantation proceedings. 2007;39(4):927-9.
71. Abuhab A, Trindade E, Aulicino GB, Fujii S, Bocchi EA, Bacal F. Chagas' cardiomyopathy: the economic burden of an expensive and neglected disease. International journal of cardiology. 2013;168(3):2375-80.
72. Irlam J, Mayosi BM, Engel M, Gaziano TA. Primary prevention of acute rheumatic fever and rheumatic heart disease with penicillin in South African children with pharyngitis: a cost-effectiveness analysis. Circ Cardiovasc Qual Outcomes. 2013;6(3):343-51.
73. Reeves BM, Kado J, Brook M. High prevalence of rheumatic heart disease in Fiji detected by echocardiography screening. Journal of paediatrics and child health. 2011;47(7):473-8.
74. Soudarssanane MB, Karthigeyan M, Sahai A, Srinivasan S, Rao KS, Balachander J. Rheumatic fever and rheumatic heart disease: primary prevention is the cost effective option. Indian Journal of Pediatrics. 2007;74(6):567-70.
75. Wang X, Li W, Li X, An N, Chen H, Jan S, et al. Effects and cost-effectiveness of a guidelineoriented primary healthcare hypertension management program in Beijing, China: results from a 1-year controlled trial. Hypertens Res. 2013;36(4):313-21.
76. Zubair Tahir M, Enam SA, Pervez Ali R, Bhatti A, ul Haq T. Cost-effectiveness of clipping vs coiling of intracranial aneurysms after subarachnoid hemorrhage in a developing country--a prospective study. Surgical neurology. 2009;72(4):355-60; discussion 60-1.
77. Birabi BN, Oke KI, Dienye PO, Okafor UC. Cost burden of post stroke condition in Nigeria: a pilot study. Global journal of health science. 2012;4(6):17-22.

78. Kabadi GS, Walker R, Donaldson C, Shackley P. The cost of treating stroke in urban and rural Tanzania: A 6-month pilot study. African Journal of Neurological Sciences. 2013;32(2).
79. Kwatra G, Kaur P, Toor G, Badyal DK, Kaur R, Singh Y, et al. Cost of stroke from a tertiary center in northwest India. Neurology India. 2013;61(6):627-32.
80. Araujo DV, Tavares LR, Verissimo R, Ferraz MB, Mesquita E. Cost of Heart Failure in the Unified Health System. Arquivos Brasileiros de Cardiologia. 2005;84(5).
81. Zhang Y, Sun J, Pang Z, Gao W, Sintonen H, Kapur A, et al. Evaluation of two screening methods for undiagnosed diabetes in China: an cost-effectiveness study. Prim Care Diabetes. 2013;7(4):275-82.
82. Bahia LR, Araujo DV, Schaan BD, Dib SA, Negrato CA, Leao MP, et al. The costs of type 2 diabetes mellitus outpatient care in the Brazilian public health system. Value Health. 2011;14(5 Suppl 1):S137-40.
83. Abdulganiyu G, Fola T. What is the cost of illness of type II Diabetes Mellitus in a Developing Economy? International Journal of Pharmacy and Pharmaceutical Sciences. 2014;6 (Suppl. 2):927-31.

Tables and Figures

Figure 1: Article Selection Flow Chart

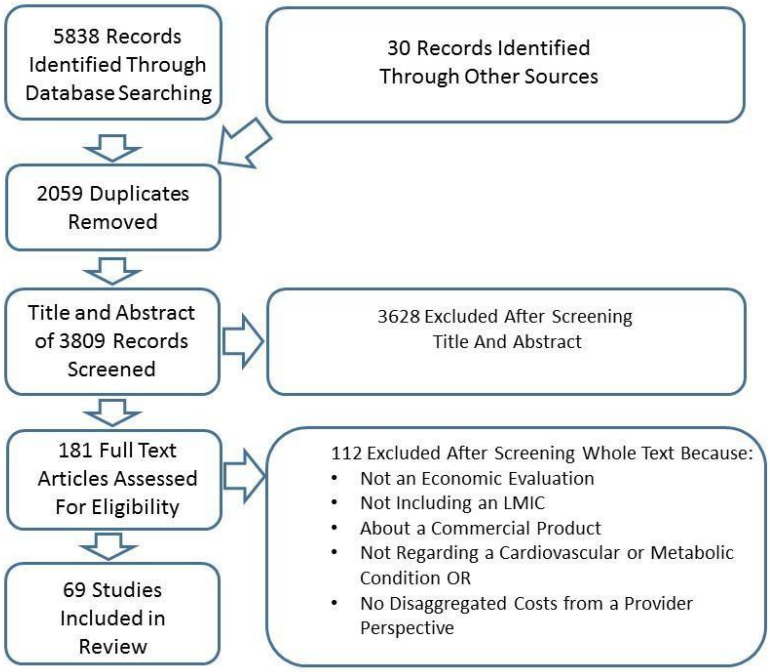


Figure 2: Articles Published By Year & Region

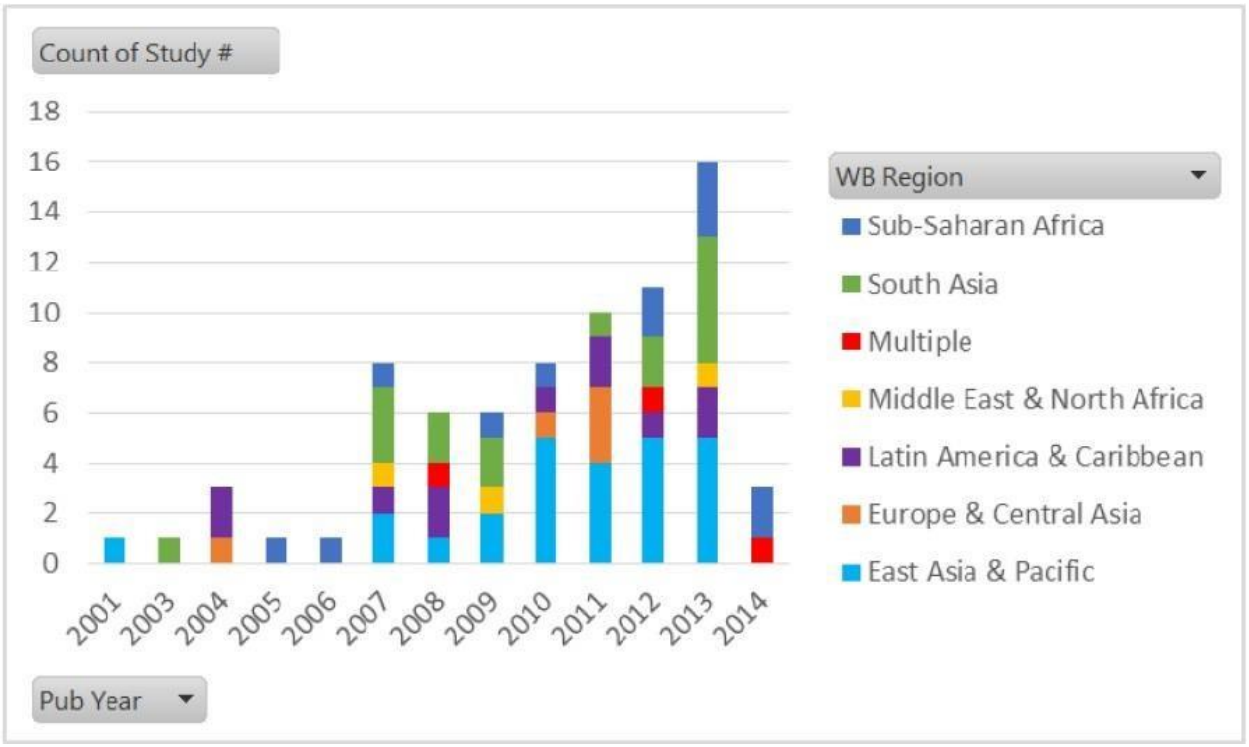
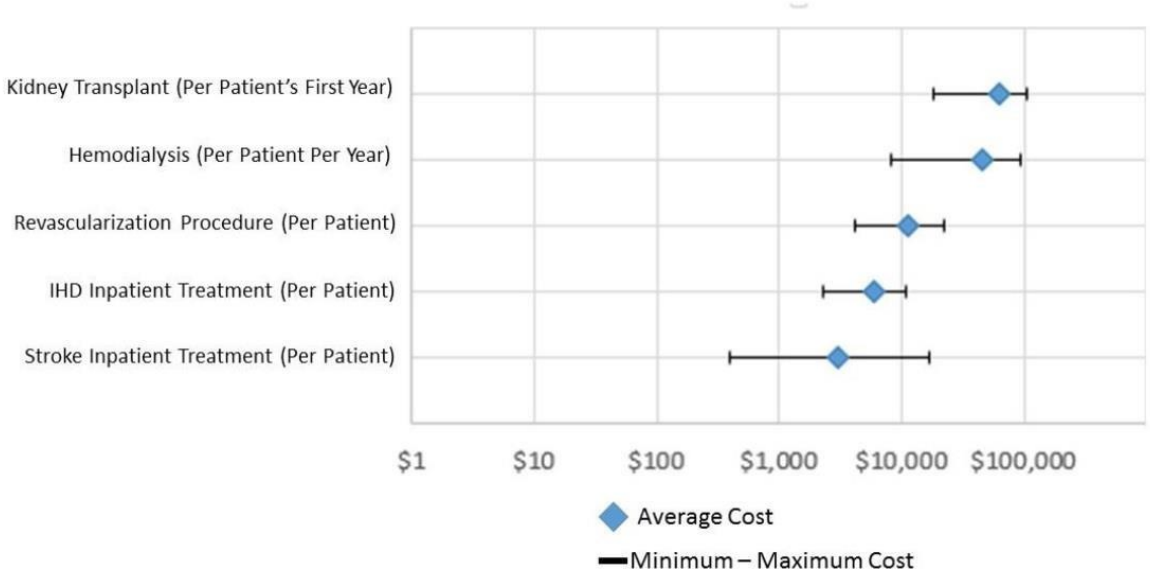


Figure 3: Hospital Costs by Condition (USD 2012)



DCP3 Disease Control Priorities
economic evaluation for health

Table 1: Total Costs of Preventive Care and Treatment of Cardiovascular Disease, Diabetes, and Kidney Disease

Category	Intervention or Treatment	Country	Cost Presented in Paper	Unit	Currency (Year)	Cost in USD (2012)	Unit
Prevention of Cardiovascular Disease, Diabetes & Kidney Disease							
Individual Level							
Primary Prevention of CVD	Community Hypertension Control Program: Home Health Education and General Practitioner(24)	Pakistan	3.99	Per patient per year	US (2007)	$4.96	Per patient per year
	Community Hypertension Control Program: Home Health Education(24)	Pakistan	3.34	Per patient per year	US (2007)	$4.15	Per patient per year
	Community Hypertension Control Program: General Practitioner(24)	Pakistan	0.65	Per patient per year	US (2007)	$0.81	Per patient per year
	Community Hypertension Reduction Program (1year)(25)	China	7.17	Per patient per year	US (2009)	$8.67	Per patient per year
	Guideline-Oriented Training Program for Hypertension Control in Community Health Centers(75)	China	79.30	Per year	US (2002)	$138.96	Per year
Secondary Prevention of CVD	Screening for dyslipidemia as secondary prevention among healthy 35-39 year olds(26)	Thailand	127.22	Per patient screened	Thailand (2008)	$4.48	Per patient screened
	Screening for dyslipidemia as secondary prevention among healthy 35-60 year olds(27)	Thailand	1,043.60	Per case detected	Thailand (2008)	$36.77	Per case detected
	Home visit by Health Care Professional(30)	Thailand	574.86	Per visit	Thailand (1999)	$25.98	Per visit
	Bupropion treatment for tobacco cessation(28)	Argentina	117.15	Per patient per year	US (2007)	$123.09	Per patient per year
Type 2 Diabetes	Conventional Glycemic Control(17)	Mexico	423,000,000.00	Per year (total country)	$Int (2005)	$0.59	Per capita per year
Stroke	Secondary Prevention(17)	Mexico	117,000,000.00	Per year (total country)	$Int (2005)	$0.16	Per capita per year

Heart Failure	Heart Failure Interventions (all)(17)	Mexico	18,000,000.00	Per year (total country)	$Int (2005)	$0.03	Per capita per year
Rheumatic Heart Disease	Primary prevention (including culturing and screening sore throats)(74)	India	1,088.56	Per patient	India (2007)	$32.61	Per patient
	Secondary Prevention (treating rheumatic fever)(74)	India	879.35	Per patient	India (2007)	$26.35	Per patient
	Tertiary Prevention (inpatient care, surgery, etc)(74)	India	1,547.17	Per patient	India (2007)	$46.35	Per patient
Population Level							
Tobacco Cessation	Graphic Warning Label on Pack(16)	Vietnam	1,492,000,000.00	Per 10 years	Vietnam (2008)	0.00013	Per capita per year
	Mass Media Campaign(16)	Vietnam	147,559,000,000.00	Per 10 years	Vietnam (2008)	$0.01	Per capita per year
	Smoking Ban (Public/Work)(16)	Vietnam	213,850,000,000.00	Per 10 years	Vietnam (2008)	$0.02	Per capita per year
	Tax increase and advertisement ban(17)	Mexico	26,000,000.00	Per year (total country)	$Int (2005)	$0.04	Per capita per year
	School program implementation- 2 years(15)	India	7,261.00	Per school	US (2006)	$10,484.16	Per school
	School program teacher and volunteer training(15)	India	2,020.00	Per school	US (2006)	$2,916.68	Per school
Health Promotion	Annual Program Costs of Shutting down street to motor vehicles to promote physical activity(23)	Mexico	10.66	Per participant	US (2010)	$11.01	Per participant
	Annual Program Costs of Shutting down street to motor vehicles to promote physical activity(23)	Colombia	2.34	Per participant	US (2010)	$2.64	Per participant
	Media campaign to reduce either salt, tobacco or cholesterol(14)	Vietnam	89,000,000,000.00	Per year	Vietnam (2007)	$0.09	Per capita per year

	Mass media combination to reduce consumption of salt and tobacco and reduce cholesterol levels(14)	Vietnam	167,000,000,000.00	Per year	Vietnam (2007)	$0.18	Per capita per year
	School-based program - Nutrition Intervention(22)	China	7.80	Per participant	US (2010)	$9.05	Per participant
	School-based program - Physical Activity Intervention(22)	China	7.70	Per participant	US (2010)	$8.94	Per participant
	School-based program - Combined Nutrition & Physical Activity Intervention(22)	China	27.18	Per participant	US (2010)	$31.55	Per participant
Salt Reduction	Population salt reduction by 30%(17)	Mexico	11,000,000.00	Per year (total country)	$Int (2005)	$0.02	Per capita per year
	Health Promotion Campaign to Reduce Salt Intake(18)	Tunisia	101,407.00	Per year	$Int (2010)	$0.02	Per capita per year
	Labelling and monitoring food packaging (18)	Tunisia	67,030.00	Per year	$Int (2010)	$0.01	Per capita per year
	Mandatory salt reduction of processed foods (reformulation) and monitoring(18)	Tunisia	136,951.00	Per year	$Int (2010)	$0.02	Per capita per year
	Health Promotion Campaign to Reduce Salt Intake(18)	Turkey	5,287,500.00	Per year	$Int (2010)	$0.08	Per capita per year
	Labelling and monitoring food packaging (18)	Turkey	120,452,534.00	Per year	$Int (2010)	$1.72	Per capita per year
	Mandatory salt reduction of processed foods (reformulation) and monitoring(18)	Turkey	198,690,082.00	Per year	$Int (2010)	$2.84	Per capita per year
Type 2 Diabetes	Diet or exercise intervention in a community(19)	China	362.00	Per patient per year	US (2007)	$512.70	Per patient per year

	Both diet and exercise intervention in a community(19)	China	371.00	Per patient per year	US (2007)	$525.45	Per patient per year
	Community-level program conducting diabetes risk score(21)	China	5.40	Per 1000 people per year	Euro area (2010)	$8.30	Per 1000 people per year
	Health Promotion and Informational Booklet(21)	China	31.30	Per 1000 people per year	Euro area (2010)	$48.11	Per 1000 people per year
	Diabetes Prevention Newspaper Articles(21)	China	7.70	Per 1000 people per year	Euro area (2010)	$11.84	Per 1000 people per year
	Diabetes Prevention Radio Ads(21)	China	37.50	Per 1000 people per year	Euro area (2010)	$57.64	Per 1000 people per year
	Nationwide population screening program for diabetes (citizens 40+): Capillary glucose screening tests through the national healthcare system(20)	Brazil	76.00	Per case detected	US (2001)	$183.06	Per case detected
Treatment of Cardiovascular Disease, Diabetes & Kidney Disease							
Ischemic Heart Disease							
Ischemic Heart Disease	CABG Procedure (Procedure and Medical Therapy)(31)	South Africa	11,431.00	Per patient	US (2001)	$22,500.46	Per patient
therapy)(36)	CABG Procedure (Procedure only, no medical	China	7,300.00	Per patient	US (2007)	$10,339.01	Per patient
	CABG Procedure (Procedure and Medical Therapy)(38)	Armenia	3,368.19	Per patient	US (2005)	$5,546.46	Per patient
	CABG Procedure (Procedure and Medical Therapy)(39)	India	8,055.00	Per patient	US (2006)	$11,630.62	Per patient
	Stenting Procedure (Procedure only, no medical therapy)(36)	China	10,000.00	Per patient	US (2007)	$14,163.03	Per patient

	Catheter-based revascularization Inpatient Treatment(31)	South Africa	4,737.00	Per patient	US (2001)	$9,324.18	Per patient
	Total operative procedures and examinations(37)	Brazil	444.29	Per patient	Brazil (2001)	$455.47	Per patient
	Coronary Angioplasty (CA) Diagnostic Strategy Including Therapy(36)	China	3,568.00	Per patient	US (2007)	$5,053.37	Per patient
	Computed Tomography Angiography (CTA) and Coronary Angioplasty (CA) Diagnostic Strategy(36)	China	2,971.00	Per patient	US (2007)	$4,207.84	Per patient
	Post CHD with CABG (1st year)(31)	South Africa	1,300.00	Per year	US (2001)	$2,558.88	Per year
	Post CHD with CABG (subsequent years)(31)	South Africa	600.00	Per year	US (2001)	$1,181.02	Per year
	Post CHD without CABG (1st year)(31)	South Africa	1,500.00	Per year	US (2001)	$2,952.56	Per year
	Post CHD without CABG (subsequent years)(31)	South Africa	840.00	Per year	US (2001)	$1,653.43	Per year
	Inpatient Visit (All direct medical costs)(28)	Argentina	4,245.39	Per patient	US (2007)	$4,460.54	Per patient
	Outpatient Visit (All direct medical costs)(33)	China	245.40	Per outpatient visit	China (2003)	$51.36	Per outpatient visit
	Inpatient Visit (All direct medical costs)(33)	China	11,008.20	Per inpatient stay	China (2003)	$2,304.00	Per inpatient stay
	Inpatient Visit (All direct medical costs)(40)	Vietnam	31,400,000.00	Per inpatient stay	Vietnam (2005)	$3,257.15	Per inpatient stay

Average CVD Event	Average Inpatient Treatment (All direct medical costs)(31)	South Africa	5,636.00	Per patient	US (2001)	$11,093.74	Per patient
Hospital-acquired infection	Additional cost if a CABG or valve replacement surgery results in a Hospital-acquired infection (39)	India	14,818.00	Per patient	US (2006)	$21,395.72	Per patient
Hypertension	Hypertension Outpatient Treatment(31)	South Africa	86.00	Per patient per year	US (2001)	$169.28	Per patient
	Hypertension Outpatient Treatment(32)	China	487.30	Per patient per year	US (2010)	$565.54	Per patient per year
	Hypertension Outpatient Treatment at Urban Health Clinic(30)	Thailand	916.54	Per patient per year	Thailand (1999)	$41.42	Per patient per year
	Hypertension Outpatient Treatment(33)	China	96.90	Per outpatient visit	China (2003)	$20.28	Per outpatient visit
	Hypertension Outpatient Treatment and Medications(29)	Tanzania	38.00	Per patient per year	US (2012)	$38.00	Per patient per year
	Hypertension Inpatient Visit(33)	China	3,904.00	Per inpatient stay	China (2003)	$817.10	Per inpatient stay
	Hypertension Drug Treatment (35)	Nigeria	2,100.00	Per month	Nigeria (2010)	$2.38 - $16.66	Per year
	Pharmacological high blood pressure and cholesterol treatment(34)	Tanzania	1.57	Per year	US (2005)	$2.21 - $76.29	Per year
	Pharmacological high blood pressure treatment(28)	Argentina	49.72	Per patient per year	US (2007)	$52.24	Per patient per year
	Pharmacological high cholesterol treatment(28)	Argentina	118.79	Per patient per year	US (2007)	$124.81	Per patient per year
	Modified poly-pill strategy(28)	Argentina	103.46	Per patient per year	US (2007)	$108.70	Per patient per year

	General Outpatient Visit(30)	Thailand	67.82	Per outpatient visit	Thailand (1999)	$3.07	Per outpatient visit
Stroke							
Hemorrhagic Stroke	Inpatient Visit for Stroke Care (Average 11.8 Days LOS)(41)	Turkey	1,348.00	Per patient	US (2007)	$1,444.46	Per patient
	Inpatient Visit for Stroke Care (Average 12 Days LOS)(42)	Brazil	1,831.00	Per patient	US (2007)	$2,388.33	Per patient
	Tertiary Treatment and Follow-Up - Coiling (6 months)(76)	Pakistan	304,800.00	Per patient	Pakistan (2007)	$6,236.79	Per patient
	Tertiary Treatment and Follow-Up - Endovascular clipping (6 months) (76)	Pakistan	187,620.00	Per patient	Pakistan (2007)	$3,839.06	Per patient
Ischemic Stroke	Inpatient Visit for Stroke Care (Average 10.4 Days LOS) (41)	Turkey	956.00	Per patient	US (2007)	$1,024.41	Per patient
	Inpatient Visit for Stroke Care (Average 13.3 Days LOS) (42)	Brazil	1,645.00	Per patient	US (2007)	$2,145.71	Per patient
	Inpatient Visit for Stroke Care (Average 18.5 Days LOS)(47)	China	67.00	Per patient per day	US (2010)	$77.76	Per patient
	Inpatient Visit for Stroke Care (Average 18.5 Days LOS)(47)	China	983.00	Per patient	US (2010)	$1,140.84	Per patient
	Primary prevention for high-risk patients at a tertiary hospital (48)	China	435.40	Per patient per year	US (2010)	$505.31	Per patient per year
Stroke (Non-Specified)	Direct Medical Costs for Managing a Stroke Patient in Year Following Stroke(77)	Nigeria	62,217.00	Per patient	US (2012)	$62,217.00	Per patient

	Inpatient Visit for Stroke Care: Average across all wards (3-5 Days Ave. LOS) (49)	Pakistan	1,179.00	Per patient	US (2001)	$2,160.99	Per patient
	Inpatient Visit for Stroke Care: ICU (3-5 Days LOS) (49)	Pakistan	3,583.50	Per patient	US (2001)	$6,568.20	Per patient
	Inpatient Visit for Stroke Care: Private Ward (3-5 Days LOS) (49)	Pakistan	1,248.00	Per patient	US (2001)	$2,287.46	Per patient
	Inpatient Visit for Stroke Care: General Ward (3-5 Days LOS) (49)	Pakistan	1,010.00	Per patient	US (2001)	$1,851.23	Per patient
	Inpatient Visit for Stroke Care (LOS not stated)(31)	South Africa	8,633.00	Per patient	US (2001)	$16,992.95	Per patient
	Inpatient Visit for Stroke Care (LOS not stated)(78)	Tanzania	138,000.00	Per patient	Tanzania (2006)	$160.18	Per patient
	Inpatient Visit for Stroke Care (LOS not stated)(28)	Argentina	3,455.48	Per patient	US (2007)	$3,630.60	Per patient
	Inpatient Visit for Stroke Care (Up to 3 Days LOS)(45)	Congo, Rep.	158,120.00	Per patient	Congo, Rep. (2006)	$397.19	Per patient
	Inpatient Visit for Stroke Care (LOS not stated)(33)	China	7,953.10	Per inpatient stay	China (2003)	$1,664.57	Per inpatient stay
	Inpatient Visit for Stroke Care: small hospital (Average 20 Days LOS)(44)	China	7,119.00	Per inpatient stay	China (2006)	$1,388.31	Per inpatient stay
	Inpatient Visit for Stroke Care: tertiary hospital (Average 20 Days LOS)(44)	China	12,344.00	Per inpatient stay	China (2006)	$2,407.26	Per inpatient stay
	Inpatient Visit for Stroke Care (Average 6.4 Days LOS)(43)	Malaysia	3,696.40	Per patient per admission	Malaysia (2005)	$1,431.57	Per patient per admission
	Outpatient Visit(33)	China	264.80	Per outpatient visit	China (2003)	$55.42	Per outpatient visit
	Direct Medical and follow up (6-months)(79)	India	57,381.00	Per patient	India (2011)	$1,173.80	Per patient

Heart Failure							
Chagas Cardiomyopathy	Inpatient treatment for heart failure due to systolic or diastolic dysfunction with a Chagas' cardiomyopathy diagnosis(71)	Brazil	467.00	Per day	Brazil (2006)	$324.23	Per day
Heart Failure	Inpatient treatment for heart failure due to systolic or diastolic dysfunction with Non-Chagas' cardiomyopathy (other etiologies) (71)	Brazil	308.00	Per day	Brazil (2006)	$213.84	Per day
	Inpatient Care (Up to 3 Days LOS)(45)	Congo, Rep.	81,900.00	Per patient	Congo, Rep. (2006)	$205.73	Per patient
	Inpatient Care (Average 6.5 Days LOS)(80)	Brazil	4,033.62	Per inpatient stay	Brazil (2002)	$3,812.90	Per inpatient stay
	Outpatient Treatment(80)	Brazil	14.40	Per outpatient visit	Brazil (2002)	$13.61	Per outpatient visit
	Outpatient Treatment plus medications(80)	Brazil	557.28	Per year	Brazil (2002)	$526.79	Per year
Hypertensive Emergency	Treatment Cost (Inpatient and Outpatient)(45)	Congo, Rep.	159,600.00	Per patient	Congo, Rep. (2006)	$400.90	Per patient
Neglected Heart Diseases							
Congenital heart disease	Operations and treatments, including pre and postoperative care(37)	Brazil	1,428.05	Per patient	Brazil (2001)	$1,463.95	Per patient
Rheumatic Fever	Inpatient Treatment (LOS not stated)(72)	South Africa	2,958.00	Per patient	US (2010)	$2,927.41	Per patient
Rheumatic Heart Disease	Inpatient Treatment (Average 7 Days LOS)(72)	South Africa	1,597.00	Per patient	US (2010)	$1,580.49	Per patient

	Use of an Echocardiogram to screen students in a school-based screening program(73)	Fiji	2.07	Per patient screened	US (2008)	$2.27	Per patient screened
	Use of an Echocardiogram to screen students in a school-based screening program(73)	Fiji	37.55	Per case detected	US (2008)	$41.12	Per case detected
Type Two Diabetes Mellitus							
Type 2 Diabetes	Inpatient stay w/o hypertension (Average 7 Days LOS)(58)	India	18,650.00	Per inpatient stay	India (2007)	$558.77	Per inpatient stay
	Inpatient Stay w/hypertension (Average 5 Days LOS)(58)	India	21,000.00	Per inpatient stay	India (2007)	$629.18	Per inpatient stay
	Inpatient stay w/o hypertension (Average 7 Days LOS)(58)	India	28,000.00	Per two years	India (2007)	$419.45	Per year
	Inpatient Stay w/hypertension (Average 5 Days LOS)(58)	India	38,000.00	Per two years	India (2007)	$569.25	Per year
	Mean total annual direct medical cost (without complication)(63)	China	5,313.20	Per year	China (2007)	$989.16	Per year
	Mean total annual direct medical cost (with complication)(63)	China	13,320.10	Per year	China (2007)	$2,479.82	Per year
	Inpatient Treatment: without complication (Average 9.8 Days LOS)(61)	China	6,903.93	Per patient	China (2006)	$1,346.37	Per patient
	Inpatient Treatment: with chronic complications (Average 9.8 Days LOS)(61)	China	7,193.15	Per patient	China (2006)	$1,402.77	Per patient
	Amlodipine (Anti-hypertensive Drug Therapy for Patients with Diabetes, Hypertension, and Nephropathy)(69)	China	2,013.00	Per year	US (2004)	$3,356.78	Per year
	Irbesartan (Anti-hypertensive Drug Therapy for Patients with Diabetes, Hypertension, and Nephropathy) (69)	China	1,660.00	Per year	US (2004)	$2,768.13	Per year
	Amlodipine (Anti-hypertensive Drug Therapy for Patients with Diabetes, Hypertension, and	Malaysia	332.00	Per year	US (2004)	$503.07	Per year

	Nephropathy) (69)						
	Irbesartan (Anti-hypertensive Drug Therapy for Patients with Diabetes, Hypertension, and Nephropathy) (69)	Malaysia	258.00	Per year	US (2004)	$390.94	Per year
	Amlodipine (Anti-hypertensive Drug Therapy for Patients with Diabetes, Hypertension, and Nephropathy) (69)	Thailand	779.00	Per year	US (2004)	$1,302.06	Per year
	Irbesartan (Anti-hypertensive Drug Therapy for Patients with Diabetes, Hypertension, and Nephropathy) (69)	Thailand	1,340.00	Per year	US (2004)	$2,239.75	Per year
	Inpatient/ Hospital Admission(55)	Thailand	95.99	Per day	US (2008)	$112.65	Per day
	Outpatient Care(55)	Thailand	3.94	Per outpatient visit	US (2008)	$4.63	Per outpatient visit
	Annual Diabetes Treatment in Community Clinic (Including Inpatient and Outpatient Visits)(56)	Brazil	1,319.15	Per year	US (2010)	$1,335.52	Per year
	Inpatient Treatment in Community Clinic (No LOS Stated)(56)	Brazil	26.32	Per year	US (2010)	$26.65	Per year
	Outpatient Care in Community Clinic(56)	Brazil	1,216.33	Per year	US (2010)	$1,231.43	Per year
complications (57)	Outpatient treatment for patient without	India	4,493.00	Per year	India (2009)	$112.05	Per inpatient stay
	Outpatient Treatment (59)	Nepal	16.95	Per outpatient visit	US (2010)	$17.45	Per outpatient visit

	Outpatient Treatment (59)	Nepal	130.52	Per year	US (2010)	$134.38	Per year
	Screening using Fasting capillary blood glucose(81)	China	10.00	Per test	China (2009)	$1.77	Per test
	Screening using Diabetes Risk Score (81)	China	5.00	Per test	China (2009)	$0.89	Per test
	Tertiary Hospital Diagnostic Test(81)	China	95.00	Per test	China (2009)	$16.82	Per test
	Primary Care - Behavior management program to prevent diabetes(62)	India	54.67	Per patient per year	US (2006)	$78.93	Per patient per year
	Primary Care - Metformin regimen to prevent diabetes (62)	India	53.00	Per patient per year	US (2006)	$76.53	Per patient per year
	Primary Care - Behavior management program with Metformin regime to prevent diabetes(62)	India	69.67	Per patient per year	US (2006)	$100.59	Per patient per year
	Outpatient Treatment(82)	Brazil	1,014.00	Per patient per year	US (2007)	$1,322.64	Per patient per year
	Annual treatment costs (inpatient and outpatient costs)(66)	Thailand	6,331.00	Per patient per year	Thailand (2001)	$277.14	Per patient per year
	Annual treatment costs (inpatient and outpatient costs)(83)	Nigeria	47,924.36	Per patient per year	Nigeria (2010)	$380.14	Per patient per year
	Annual treatment costs (inpatient and outpatient costs)(64)	India	3,006.00	Per patient per year	India (2012)	$56.25	Per patient per year
	Outpatient Treatment(60)	Pakistan	1,468.90	Per outpatient visit	Pakistan (2006)	$32.34	Per outpatient visit
	Screening for diabetes in a community health clinic(19)	China	3.00	Per patient	US (2007)	$4.25	Per patient
	Urban Health Center providing primary community care(30)	Thailand	1,408.59	Per patient per year	Thailand (1999)	$63.66	Per outpatient visit

	Outpatient Visit (33)	China	163.80	Per outpatient visit	China (2003)	$34.28	Per outpatient visit
	Inpatient Visit (No LOS Stated)(33)	China	6,045.50	Per inpatient stay	China (2003)	$1,265.31	Per inpatient stay
Diabetic Foot Ulcers	Treatment(50)	Pakistan	2,700.00	Per patient	Pakistan (2005)	64.15 - $1165.65	Per patient
	Total Treatment (healed)(51)	China	1,673.00	Per patient	$Int (2010)	$585.60	Per patient
	Total Treatment (trans-tibial amputation)(51)	China	21,372.00	Per patient	$Int (2010)	$7,480.87	Per patient
	Total Treatment (healed)(51)	India	1,192.00	Per patient	$Int (2010)	$85.51	Per patient
	Total Treatment (trans-tibial amputation)(51)	India	19,599.00	Per patient	$Int (2010)	$1,405.97	Per patient
	Total Treatment (healed)(51)	Tanzania	102.00	Per patient	$Int (2010)	$0.24	Per patient
	Total Treatment (trans-tibial amputation)(51)	Tanzania	3,060.00	Per patient	$Int (2010)	$7.30	Per patient
	Diabetic foot treatment, total(52)	Nigeria	93,256.70	Per patient	Nigeria (2003)	$1,618.55	Per patient
Retinopathy	Retinopathy screening in a primary care setting(53)	South Africa	22.00	Per patient	US (2007)	$26.10	Per patient
	Laser treatment in retinopathy confirmed cases(53)	South Africa	144.00	Per patient	US (2007)	$170.85	Per patient

	Screening Retinal examination at a hospital(54)	India	5.84	Per patient	US (2009)	$7.05	Per patient
	Screening single laser photocoagulation treatment at a hospital(54)	India	7.51	Per patient	US (2009)	$9.07	Per patient
	Screening Using Telescreening in rural areas(54)	India	7.36	Per patient	US (2009)	$8.88	Per patient
Chronic Kidney Disease							
End Stage Renal Disease	Dialysis(69)	China	56,584.00	Per year	US (2004)	$94,356.62	Per year
	Renal Transplant (first year expenses)(69)	China	54,886.00	Per year	US (2004)	$91,525.12	Per year
patient(69)	Maintenance post index year of transplant	China	27,259.00	Per year	US (2004)	$45,455.73	Per year
	Dialysis(69)	Malaysia	19,054.00	Per year	US (2004)	$28,871.91	Per year
	Renal Transplant (first year expenses)(69)	Malaysia	70,022.00	Per year	US (2004)	$106,102.06	Per year
	Maintenance post index year of transplant patient(69)	Malaysia	14,111.00	Per year	US (2004)	$21,381.94	Per year
	Dialysis(69)	Thailand	31,651.00	Per year	US (2004)	$52,903.20	Per year
	Renal Transplant (first year expenses)(69)	Thailand	45,953.00	Per year	US (2004)	$76,808.34	Per year
	Maintenance post index year of transplant patient(69)	Thailand	19,349.00	Per year	US (2004)	$32,340.97	Per year
	1 session of hemodialysis in a hospital(67)	Jordan	72.00	Per session	US (2010)	$78.76	Per session
	Hemodialysis maintenance session in a hospital(65)	Iran, Islamic Rep.	52.60	Per session	US (2007)	$96.66	Per session

Kidney failure	Hemodialysis in a hospital(68)	Sudan	15,747.68	Per patient per year	Sudan (2009)	$8,374.01	Per patient per year
	Hemodialysis in a hospital(68)	Sudan	146.58	Per patient per session	Sudan (2009)	$77.95	Per patient per session
	Kidney transplantation, including operation and following year(68)	Sudan	34,097.85	Per patient	Sudan (2009)	$18,131.93	Per patient
	Kidney transplantation, after the first year(68)	Sudan	24,499.00	Per patient	Sudan (2009)	$13,027.63	Per patient
	Transplantation Procedure(70)	Iran, Islamic Rep.	2,048.00	Per patient	US (2005)	$4,769.20	Per patient
	Total cost (Procedure, 1 year immunosuppression, donor costs)(70)	Iran, Islamic Rep.	9,224.00	Per patient	US (2005)	$21,480.05	Per patient