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# **The Economic Costs of Cardiovascular Disease, Diabetes Mellitus and Associated Complications in South Asia: A Systematic Review**

## **ABSTRACT**

**Background:** Over 80% of global deaths caused by cardiovascular disease (CVD) and diabetes (DM) occur in developing countries. The burden of non-communicable disease (NCDs) in South Asia is increasing rapidly.

**Objectives:** To estimate the costs of CVD and the costs of DM to individuals and society in Afghanistan, Bangladesh, Bhutan, India, Maldives, Nepal, Pakistan and Sri Lanka.

**Methods:** We systematically searched six health and economic databases for studies identifying costs related to CVD or DM and their respective complications. Costs were extracted from included studies and converted to US\$ for the price year 2015 to enable meaningful comparisons.

**Results:** Of the 71 articles suitable for full text review, 29 studies met the inclusion criteria. The majority were cost of illness studies (n=27) and were from the patient perspective (n=23). Most collected data since 2000 (n=23) and included data from India (n=24). No studies included longitudinal costs at the patient level. Medical costs for routine management of CVD and DM were broadly similar. These costs escalate significantly once complications occur which require treatment, particularly for stroke, major coronary events and amputations. Costs are mainly borne by the individual and family. Some included studies modelled rapidly rising future costs. The majority of studies included had methodological weaknesses.

**Conclusions:** Marked increases in costs have been identified when complications of these chronic diseases occur, underlining the importance of secondary prevention approaches in disease management in South Asia. Higher quality studies, especially those that include longitudinal costs, are required to establish more robust cost estimates.

## **INTRODUCTION**

The prevalence of non-communicable diseases (NCDs) such as cardiovascular disease (CVD) and diabetes mellitus type 2 (DM) is increasing worldwide, especially in low and middle income countries(1) (LMICs). Ischaemic heart disease was the single biggest cause of disability adjusted life years in the global burden of disease study(2) with an estimated 31% of all worldwide deaths being due to CVD(3).

The south Asia region has a population of 1.7 billion people, which has tripled since 1950. Life expectancy in the region has increased dramatically from 39 in 1950 to 65 years today. India's population is by far the largest, with three-quarters of the region's total(4). Along with the global trend, the prevalence of CVD and DM in the region is expected to continue to increase in the coming years(5). In South Asia, some of the main drivers for this expected rise are economic transition, urbanisation and lifestyle changes(6). The burden of disease is shifting from infectious, maternal and childhood diseases to non-communicable diseases. This epidemiological transition has occurred

rapidly and CVD, DM and their complications now contribute a significant burden of disease in these LMICs(7). For example, in India CVDs are now the leading cause of death in men and women in both rural and urban areas(1, 8). In addition, India is now the country with the second largest number of people living with diabetes at 65.1 million (second only to China at 98.4 million).

According to the World Bank(9), the south Asian region has been the fastest growing economic region in recent years. In 2015 the combined GDP of all countries in the region was US\$ 2,689,862million. By far the largest economy in the region is India (2015 GDP US\$ 2,088,841million). Other economies include Pakistan (US\$ 271,050million), Bangladesh (US\$ 195,079million), Sri Lanka (US\$ 82,316million), Nepal (US\$ 21,195million), Afghanistan (US\$ 19,331million), Maldives (US\$ 3,435million) and Bhutan (US\$ 2,058million).

Chronic diseases have a significant health impact on individuals and their families. Analysis of NCDs in South Asia highlights that while the burden is currently greatest among affluent groups, many adverse risk factors are concentrated among the poor portending future increases amongst those with the least resources to manage their condition(10). The International Diabetes Foundation (IDF) estimated diabetes related health care expenditure in 2014 to be approximately US\$6.9 billion in the South Asia region(11). With limited capacity within the public health system to effectively identify and manage CVD and DM, healthcare costs are usually borne as out of pocket expenditure by the individual and their families in this region, often with catastrophic financial consequences (12-14).

Although some countries in the region are beginning to explore social insurance schemes to fund healthcare expenditure, there is limited existing evidence to inform policy makers of these costs(15). A few literature reviews have been conducted, exploring some relevant aspects of this issue. Brouwer et al.'s review of provider costs related to CVD in LMICs(16) found a wide variation in costs but little evidence from low income countries. Yesudian et al.'s review(17) of the costs of DM in India found medication to be a large proportion of costs with the burden falling heaviest on the poor and urban populations. Seuring et al.'s review(18) of the economic costs of DM in relation to levels of national GDP found direct costs to be generally higher than indirect costs, with these direct costs being positively associated with a country's GDP per capita. None of these studies adequately addressed the question of all relevant economic costs, focused specifically on the South Asian region.

The aim of this systematic review, was to estimate the costs of CVD and the costs of diabetes to individuals and society, in the LMICs of the South Asia region according to the World Bank definition(19) which includes Afghanistan, Bangladesh, Bhutan, India, Maldives, Nepal, Pakistan and Sri Lanka. This review sought to identify and collate data from peer-reviewed studies to address the question: What are the economic costs related to cardiovascular disease and the economic costs related to diabetes mellitus and their complications on society, the health sector, individuals and their families in South Asia?

## **METHODS**

This review was undertaken according to the Centre for Reviews and Dissemination guidelines for systematic reviews and meta-analyses(20). A protocol was developed to plan the review which is available from the authors on request. The review is reported according to PRISMA guidelines(21).

### **Search Strategy**

In April 2015 we searched the databases listed below for studies containing costs of CVD and DM in the countries of South Asia:

- EconPapers (RePec)
- Embase Classic Embase (Ovid) 1947 to 2015 April 01
- Global Health (Ovid) 1973 to 2015 Week 12
- Ovid MEDLINE(R) 1946 to March Week 5 2015
- Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations April 01, 2015
- NHS Economic Evaluation Database : Issue 1 of 4, January 2015 (Wiley)
- WHOLIS World Health Organization Library & Information Networks for Knowledge Database

The search strategy comprised subject headings and text words identified by the project team and known relevant papers for the search concepts CVD, DM, Costs and South Asia. The CVD search concept was adapted from a Cochrane CVD review(22). Table 1 illustrates some of the terms we used, however the full search strategy can be found in the appendices. The results of the electronic searches were stored and managed in an EndNote library. Relevant references, cited in the identified studies, were also included, as well as any relevant studies that the authors already had from previous work. We did not have the financial and human resources to contact study authors.

**Insert Table 1 here**

### **Inclusion criteria**

Studies were considered as eligible for inclusion, if they related to the specified countries in the World Bank South Asia region and if they related to any aspects of “cost” in relation to CVD or DM.

Our aim was to obtain to the fullest extent possible, relevant costs related to CVD, DM and their complications. We used a broad definition of cost including all perspectives and elements of costs or economic impacts. Therefore, we included costs related to CVD or costs related to DM as incurred by service users and their families, service providers, governmental organisations and society. We included any types of costs regardless of any categorisation made by authors including: direct, indirect and/or intangible costs. Inclusion of studies was not restricted by specific participants or settings with the aim of capturing all relevant costs of CVD, relevant costs of DM and the complications of either disease. Study designs included in the review were randomised controlled trials (RCTs); observational studies; cost-of illness studies and systematic reviews.

We included all participants diagnosed with either DM or CVD (including ischaemic heart disease, stroke, hypertension and congestive heart failure) and their complications. We also included studies that included patients with co-morbid CVD and DM. In regard to costs of diabetes, our study aims

were focused on type 2 DM. However, studies not clearly specifying which type of DM or combining results for both type 1 and 2 were included. We did not include studies exclusively looking at type 1 or gestational diabetes mellitus.

### **Exclusion criteria**

We excluded studies if there was no full text publication available; if it was a conference abstract; if it was written in a language other than English, Hindi, Urdu or Bengali; and, if it included costs that did not relate to usual care in that setting at the time (e.g. only related to costs of a novel intervention). Cost-benefit, cost-effectiveness, cost-minimisation and cost-utility analyses were not completely excluded but reviewed separately to identify possible sources of cost data. Systematic reviews were included to ensure that any relevant studies included in other reviews were also identified in ours. The systematic review itself was not included in our analysis as this would have led to double counting of data.

### **Study Selection**

Following implementation of these search strategies, the title and abstract of each identified study were reviewed by one author and the inclusion/exclusion criteria applied. The full text articles of the short-listed studies were then reviewed independently by two authors using an extraction form and quality checklist. The two sets of quality scores were then reviewed by both authors together and discrepancies discussed to agree a consensus score for each study. If the two reviewers were unable to reach consensus on the scoring, a third reviewer was asked to assess the relevant points in the study and adjudicate.

### **Data Extraction, Quality Scoring and Risk of Bias**

We developed a data extraction tool and two of the study team (FG and HE) tested it on 5 studies before it was used to extract the relevant data from the reviewed studies. The tool can be found in the appendices. Only information available in the publication was used for assessing inclusion criteria, for data extraction, and for quality assessment.

A number of different quality checklists are available in relation to economic evaluation but there is currently no universally accepted checklist that was suitable for this review. Therefore we developed a quality assessment checklist for this study, based on a review of a number of existing checklists(20, 23-30). This checklist enabled an assessment of risk of bias to be undertaken using a scoring system across 38 quality criteria. These criteria covered a full description of; methods, context and economic study design; quantification of resources and costs; currency, price year and discounting; uncertainty and sensitivity analysis; and appropriate reporting of results and conclusion. We scored the studies with 1 point for 'yes', 0.5 for 'partial' or 'unclear' and 0 for 'no' or 'NA' for each of these criteria. The total score is presented as a percentage of the available scores for each study, thus we did not score studies down for non-applicable ratings. This assumes that each criterion carries equal

weight in the overall score. We did not exclude studies for a poor quality score, however the score is presented in table 3 and should be considered in the interpretation of results.

## Summary Measures

The vast majority of studies included in this review are cost of illness studies. We reported our findings in standard health economics terms(30): medical direct costs (financial transactions for health services), non-medical costs (financial transactions for non-medical services e.g. transport), indirect costs (lost productivity) and intangible costs (disvalue to an individual such as pain or suffering). Most units of measurement are reported as mean annual cost per patient or mean annual cost per hospital admission. Once we extracted these costs from each included study, we converted them to US\$ for the price year 2015 (using Purchasing Power Parity data from the IMF), in order to enable meaningful comparisons. This was done using an online cost converter (v1.5 accessed in May 2016) designed for this purpose and found at <http://eppi.ioe.ac.uk/costconversion/> (31). We grouped our findings by disease and by the presence of complications to assist with further comparison. Where studies collected data over several years and had not been adjusted to one price year, we took the mid-year as the original price year for conversion.

As studies included in this review reported findings for different diseases, with a range of complications in a variety of settings, it was not possible for us to synthesise the data into a meta-analysis. The findings of this systematic review are therefore descriptive in nature.

## Results

We identified 1,437 articles from our searches (after duplicates had been removed). Five of these came from reference lists of other systematic reviews. Of these, 1,366 were excluded after screening titles and abstracts as not meeting our inclusion criteria. Of the remaining 71 articles that were eligible for full text review, 42 were excluded (the reasons are listed in Fig. 1) which left 29 studies to be included in our review.

Insert Fig. 1 here

### Study Characteristics (see Table 2)

The vast majority of the studies (n=27) were cost of illness studies. The two remaining studies were economic modelling studies(32, 33). Most studies assessed costs from the patient perspective (n=24) with the rest being from the societal perspective (n=5). An important gap in the evidence base is the lack of information from half of the countries, with only 4 out of the 8 South Asia countries contributing to included studies. The results will, to a degree, be Indo-centric as the majority of studies (n=23) provided data from India. The other three countries represented were Pakistan (n= 5), Bangladesh (n=1) and Nepal (n=1). Most studies were set in public or private hospitals (n=22; of which 8 were across multiple sites and 4 were outpatient departments only). Other settings included

a district/region (n=3) and nationwide settings (n=4). Most studies were quite recent, only six studies had collected data before the year 2000.

Sample sizes within the cost of illness studies ranged from 150 to 383,000 individuals, with a median sample size of 400. Twenty studies included data for DM (type 2 (n=7) or not stated (n=13); with 11 of these DM studies including complications of the disease). Eleven studies included data for CVD, of which, some included participants with DM (n=2) and some related specifically to stroke (n=3), hypertension (n=2) and angina (n=1). Of the 23 studies that reported mean age of the sample, the range of means was 49 to 70 years old. Of the 24 studies that reported on the sex ratio of the sample, males were in the majority in 20 studies (% males pooled across 24 studies = 56%).

Sources of cost data were obtained from self-reporting (n=21), hospital records (n=9), national reference costs (n=5) and international reference costs (n=2) with some studies combining several sources. As the majority were cost of illness studies it is unsurprising that the vast majority of included studies reported direct medical costs (n=28). These were mainly costs for consultation fees, medicines, lab investigations, admission charges, bed fees, surgery costs, nursing charges and rehabilitation fees. A lesser proportion of studies included direct non-medical costs (n= 17) which were mostly transport and food costs. Fewer studies still included indirect costs (n=5) which were all estimates of loss of productivity. One study included intangible costs which estimated a willingness to pay value using a bidding method. The currencies that studies reported in were Indian rupees (n=20), US dollars (n=7), Pakistan Rupees (n=4), International dollars (n=2) and pounds sterling (n=1).

Seven studies were authored by researchers from the same WHO Collaborating Centre for Research in Chennai, India(34-40) and three studies were from a study group in Bangalore(41-43). The results from our quality checklist indicate that many studies failed to report substantial elements of their methods, therefore, poor internal validity is a risk for these studies.

Insert Table 2 here

### **Risk of Bias within studies (see Table 2)**

Using our quality checklist, we identified scores for included studies that ranged between 40.9% and 89.1%. The median score was 71.0%. The distribution of scores for the 29 studies is represented in Fig. 2. Seven studies had a quality score below 60%. Five studies had a quality score exceeding 80%. There were no obviously similar study characteristics between poorly scoring studies. There was a similar range of quality scores for studies that included participants with DM compared to studies for CVD. The studies with low quality scores were spread across all diseases and study types (see table 3).

Insert Figure 2 here

### **Annual economic costs of CVD per person (see Table 3)**

There were eleven studies that estimated economic costs for CVD in some of the countries of South Asia. One study from India(44) estimated the annual direct medical cost of managing hypertension on an outpatient basis as US\$ 386. Another study from India(45) estimated the annual cost of all CVD care as US\$ 563. When patients are admitted to hospital with CVD significant costs are incurred

with a range of US\$ 677 - 1,523(33, 46, 47) per hospitalisation. Among the studies that estimated hospitalisation costs for CVD, the earlier studies tended to have lower costs than later studies (even after adjusting for price year). For the routine management of CVD, drug costs were estimated in four studies(44, 46, 48, 49). For the management of hypertension the range of annual drug costs was US\$ 79 - 231(44, 46, 48) and for CVD (defined broadly) the drug costs were estimated to be US\$ 1.14 per day, or US\$ 415 per year(49).

Given that stroke care requires significant treatment and rehabilitation as an in-patient and that all three studies that captured costs for stroke care (Pakistan=1, India=2) sampled in-patients, it is not surprising that estimates of costs were some of the highest found in this review. The range of direct medical costs associated with each stroke(50-52) was US\$ 3,890 - 28,451, with the range of direct non-medical costs being US\$ 357 - 1,552. Along with direct costs, indirect costs for transport and home adaptations for stroke were also substantial; estimated at US\$ 872 – 1,719 per hospitalisation(51, 52). Overall costs of each stroke from a societal perspective were estimated(51, 52) to be US\$ 5,966 - 32,927. Given that the included studies only captured post-stroke data for 6 or 12 months, the longer term cost to society is likely to be substantially more (particularly indirect costs).

From a societal perspective the direct and indirect costs of CVD are considerable. Direct medical costs for CVD were estimated(33) to be US\$ 10.2 billion for India in 2004. This data was then projected for the years 2016 and 2021 as US\$ 14.4 billion and US\$ 16.6 billion respectively which suggests a significant rise, in line with the growth in both population and prevalence. The authors emphasise that this impact falls predominantly on the working age population. Another study(32) modelled the estimated indirect costs of loss of productivity to the economies of India, Pakistan and Bangladesh, from CVD in 2015, which were estimated to be US\$ 1.96 billion, US\$ 0.21 billion and US\$ 0.14 billion respectively.

### **Annual economic costs of DM per person (see Table 3)**

There were eighteen studies that estimated costs for DM in some of the countries of South Asia. Estimated costs for DM differed in terms of the type of costs that were included. Where costs were limited to outpatient care(41-43, 53-55) a range of US\$ 463 - 951 was found for mean direct medical costs. In studies that disaggregated these totals further for sub-samples within their data, the range of costs increased. For instance one study(55) in India reported that patients that used a Government funded outpatient service (compared to a private outpatient service) had lower costs at US\$ 212 and a different study(35) identified mean direct costs of US\$ 1,046 for urban patients and US\$ 655 for rural patients. When hospital admissions were included in direct medical costs the range of mean direct medical costs rose slightly to US\$ 575 - 1216(37, 43, 53, 56). However the largest direct medical costs reported by studies(40, 57, 58) were for DM patients with complications, which had a range of US\$ 246 – 4,597. The studies(57, 58) reported that complications with lower costs (US\$ 246 – 502) were nephropathy and peripheral vascular complications such as minor foot ulcers. Higher costs (US\$ 2,087 – 4,597) related to severe foot ulcers, amputations and coronary events.

Similar patterns to direct medical costs were seen for direct non-medical costs; with lowest costs for DM patients seen in outpatients only(54, 55) (range US\$ 12 – 21) with higher costs for those who



were also admitted to hospital(53) (US\$ 258) and a greater range for those with complications(34, 36, 39, 40) (cost per admission range US\$ 50 – 470). A wide range of mean annual indirect costs were estimated by studies(39, 41, 43, 53-55) for DM and its complications which ranged from US\$ 9 up to US\$ 2,803.

One study(39) estimated intangible costs for DM, as a willingness to pay, using a bidding method. This study found that on average patients were willing to pay US\$1,936 a year to stay well. However, there was a significant range when broken down by number of complications (US\$ 1,452 for no complications to US\$ 7,260 for >4 complications) and by HbA1c level (US\$ 484 for HbA1c <7 to US\$ 1,936 for HbA1c >9).

When combining costs to obtain an overall estimate, costs similarly varied. A number of studies(34, 36, 40) modelled 2 year expenditure estimates based on their data for total direct costs (medical and non-medical) which included data for serious complications of DM. The range of these 2 year costs were US\$ 2,420 to US\$ 40,331 (or annual costs of US\$ 1,210 – 20,166). Estimates from studies that additionally included indirect costs (to direct costs) tended to have much lower estimates as they were outpatient only or mixed outpatient and inpatient samples with fewer complications and so attracted lower costs. The range of total annual (direct and indirect) costs for these studies(41, 43, 54, 55, 59) was US\$ 483 – 2,637. The study(39) that estimated costs incorporating direct, indirect and intangible costs estimated annual total costs of US\$ 2,048.

**Insert table 3 here**

## **Discussion**

Our review found broadly similar estimates of annual direct medical costs per person in South Asia for routine management of CVD compared with routine management of DM, with costs of US\$ 386 for hypertension, US\$ 563 for CVD and US\$ 463 – 951 for DM outpatient care and US\$ 575 – 1216 for all DM care. Importantly, when complications (such as stroke, severe foot ulcers, amputations and coronary events) of these diseases occurred and required treatment, there was a substantial increase in costs. For severe complications of DM the direct medical costs rose to US\$ 2,087 – 4,597. For the occurrence of each stroke, direct medical costs were estimated to be US\$ 3,890 - 28,451. These findings indicate that the financial burden of treating the complications of CVD and DM in South Asia form a significant proportion of the overall financial burden of these diseases. Total annual direct costs for CVD in India have been modelled at US\$14.4 billion in 2016, which is set to increase to US\$16.6 billion by 2020. An economic imperative therefore clearly exists for policy makers in South Asia to increase preventative approaches, both to decrease the incidence of DM and CVD and to increase early detection as well as provide access to evidence based treatments in order to reduce the prevalence of costly complications.

The economic burden of these considerable direct costs borne by the patient as out-of-pocket expenditure (and increasingly by social insurance schemes) in the region is compounded by the indirect costs to individuals and families. Our review has identified total annual costs (direct and

indirect) of US\$ 1,210 – 20,166 per person for DM and US\$ 5,966 – 32,927 for each patient suffering a stroke. At the national level an estimate of total economic burden of DM in India was US\$ 99.2 billion to US\$148.2 billion. This economic burden at the societal level is set to grow considerably across South Asia as the rapid epidemiological transition is set to continue. The recent increases in rates of smoking amongst the young, sedentary lifestyles and the consumption of added sugars and processed carbohydrates are projected to continue, increasing the prevalence of CVD and DM(62, 63). The ability of countries in the region to address this rising burden will depend on their commitment to preventative economic and health policies such as taxation, education, food labelling and health promotion in schools(64, 65).

Insert Table 4 here

The quality checklist that we developed for this study provided a wide range of quality scores for the included studies in our review. Studies with higher quality scores (>70%) tended to be those using more sophisticated research methods such as macro-economic modelling, multi-country data collection or estimation of indirect or intangible costs. Conversely, cost of illness studies had a wide range of quality scores with some scoring very poorly. The findings from our quality checklist support the criticism of cost of illness studies, concerning their variable results and lack of reliability due to the heterogeneity of methods employed(66). In order to improve the value of cost of illness studies, researchers should ensure they employ a robust methodological approach and follow recognised reporting standards (such as the CHEERS statement(28)). The main limitations of studies were: the inadequate description of the study population and therefore uncertainty about their representativeness; a lack of categorisation into commonly used economic categories (direct medical, direct non-medical, indirect and intangible costs); the unit costs and the sources of cost data were often not stated; the quantity of resource utilisation was not usually reported separately to the cost data; the perspective taken for the study was not often specified; and there was a lack of clarity about who bore the payment for costs identified.

The time horizon for most studies was a single year. No studies presented longitudinal costs. Given the chronicity of CVD and DM this is an important consideration. As life expectancy increases across South Asia(19) patients can expect to live longer with these diseases with increasing risks of developing associated complications and therefore an escalation of related health care costs. It is unclear how accurate these annual estimates are for cumulative costs for patients and society over the individual's life. Studies that calculate costs of CVD and DM over the medium to long term in South Asia would be welcomed.

### **Limitations**

There are several limitations to our review. Firstly, the results are dominated by studies from India. No studies provided data for Sri Lanka, Maldives, Afghanistan and Bhutan so the findings cannot easily be generalised to the region as a whole. Secondly, we only reviewed published literature and therefore some relevant data in grey literature (including non-indexed regional journals) may have been missed, limiting the comprehensiveness of our review. Thirdly, we did not contact authors to

obtain clarifying information, which may have enriched the included data and subsequent findings. Lastly, we did not exclude studies from our review based on a low quality score from our checklist, so the internal validity of some studies is questionable. However, we have presented the quality scores to allow readers to interpret results accordingly. We recognise the limitations of using a checklist scoring system to assess risk of bias and the fact that all criteria carried equal weight. Further research to explore weighting these criteria and to validate the scoring system could improve this tool.

## Conclusion

This systematic review of the economic costs of CVD, DM and their associated complications in South Asia has identified significant costs to individuals and families who bear the brunt of this financial burden currently. Marked increases in costs have been identified when complications of these chronic diseases occur, underlining the importance of secondary prevention approaches in chronic disease management. This review has summarised the current available evidence. However, given the variable quality of cost of illness studies included, the findings of this review are tentative. Higher quality studies from every country across the region, especially those that include longitudinal costs, are required to establish more robust cost estimates.

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Fig 1

**Figure 1 - Flow Diagram of the Study Selection Process**

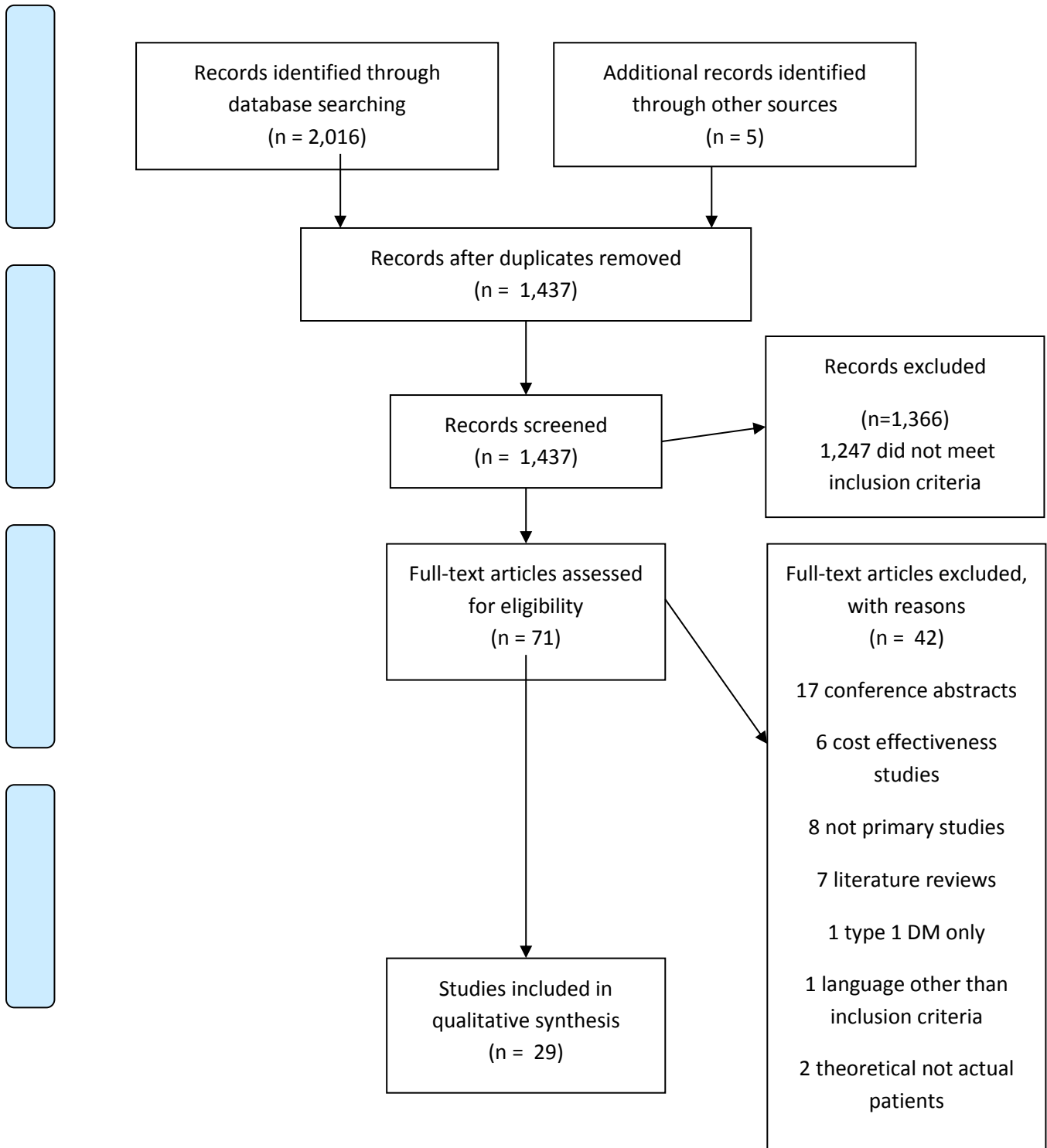


Figure 2 – Distribution of quality scores for included studies

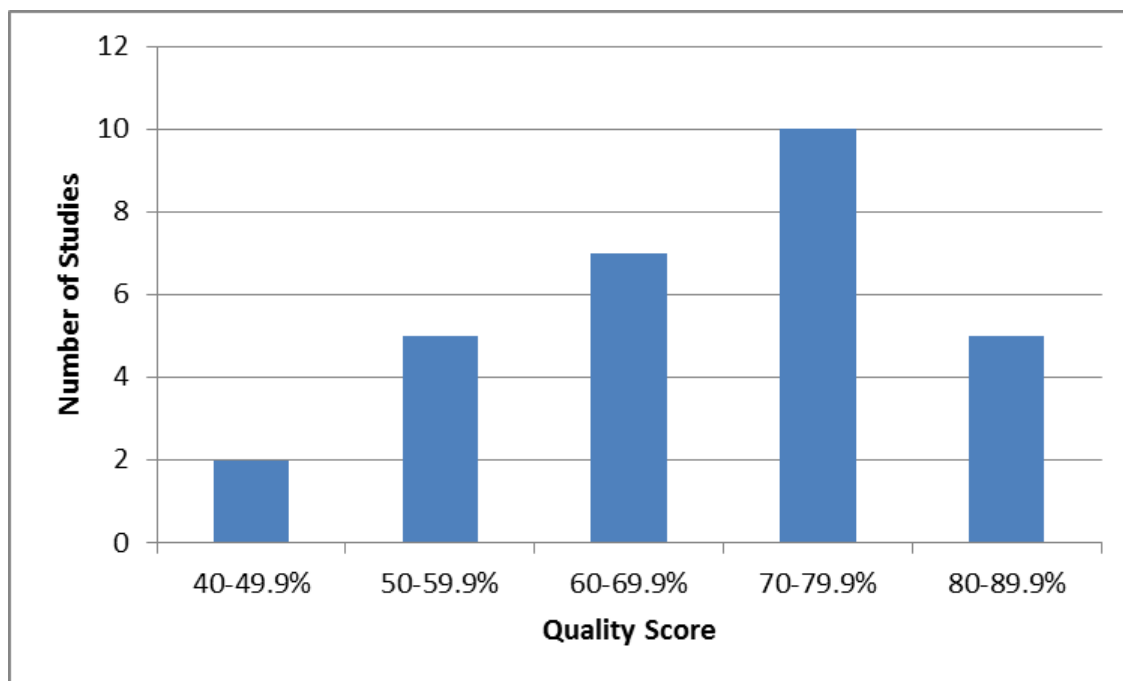


Table 1 – Example search terms used in the search strategy

Concept	Subject Headings	Text words
Diabetes Mellitus	Diabetes Mellitus/	Diabet*, niddm, mody
CVD	Cardiovascular Diseases/ Heart Diseases/ Hypertension/	Vascular diseas*, cardiovascular diseas*, stroke, thrombosis, heart attack*
South Asia	India/ Pakistan/ Bangladesh/ etc...	Indian, India, Pakistan*, Nepal*, Afghanistan*
Cost	Costs and Cost Analysis/ Budgets/	Cost* of illness, economic* burden, medical expenditure*, economic evaluation*



Table 2. Characteristics of included studies

Ref.	Country	Setting	Sample size	Sample Characteristics	Year of data collection	Condition	Includes complications	Economic Study Type & Perspective	Study type	Sources of cost data	Cost Types & Descriptions	Currency Reported
Abegunde 2007(32)	Pakistan, India, Bangladesh	National	Not applicable	Not applicable	1950-2002	CVD (Heart disease & stroke) and DM	Yes	Economic growth models; societal	Multi-country comparative analysis	Death registers, MoH surveillance, World Bank estimates, WHO disease scenarios.	Effect of premature deaths from chronic diseases on the countries' national income, which is measured in gross domestic product (GDP) losses per working-age population.	US\$
Adiga 2010(60)	India (Karnataka)	Specialty Hospital	238 patients	3 groups - mean age 57.8 - 65.5 yrs, male 43 - 57%	2008	DM type 2	Yes	Cost of illness; patient	cross-sectional case note review study	Hospital medical records department	Direct Medical cost: medicine, consultations, lab, bed charge, surgery, total annual cost during hospitalisation	Indian Rupees (INR)
Akari 2013(59)	India (Andhra Pradesh)	Speciality hospital,	150 patients	Male 67%, 24% illiterate	2012	DM	Yes	Cost of illness; patient	Case note reviews and interviews	Patient's notes; self-reporting; interviewing health-care professionals.	Direct medical costs: medication, lab, consultation, hospitalization, Direct non-medical: travel, food Indirect costs: productivity loss	INR/US\$
Ali 2008(57)	Pakistan	Specialty Hospital	214	64% male, mean age 52.7 years	1997-2004	DM (foot ulcers)	Yes Diabetic foot ulcer	Cost of illness; patient	Retrospective case note review	Hospital charges	Direct medical costs: OP consultation, investigations, medicines, hospitalization, surgery, home visits, plaster casts	Pakistan Rupees & £
Chandra 2014(53)	India (Pune)	Specialty Clinic	219 patients	Male 58.1%, Mean age 54.9 years	2011-12	DM	Yes (ophthalmology clinic)	Cost of illness; patient	Questionnaire survey and interviews	Self-reporting	Direct medical costs: medicines, doctor's fees, investigations, spectacle, laser treatment, surgery Direct non-medical costs: travel, food, dietary advice	Indian Rupees

											Indirect costs: productivity loss	
Clarke 2010(58)	India	215 clinical centres in 20 countries	471	Over 55 yr old with mean age 65.1 yrs, male 53%	2001-6	DM	yes (macrovascular)	Cost of illness; patient	Multi-country comparative analysis	WHO CHOICE economic model for bed day unit costs	Unit inpatient bed day cost per country	International \$
Hussain 2014(61)	Pakistan (Karachi)	15 different outpatient clinics at 5 sites	885 patients	male 46.2%, graduate or higher 46%	not mentioned	DM type 2	not specified	Cost of illness; patient	Patient questionnaire survey	Self-reporting	Direct medical costs : consultations, lab tests, home testing, medicine & syringes Direct non-medical: travel, food	Pakistani Rupees
Jhaj 2001(48)	India (Chandigarh)	Outpatient department (OPD) of Government Hospital	300 prescriptions (173 patients)	male 51%; mean age 53.4 (men) and 51.8 years (women).	06/1999-11/1999	Hypertension	yes, not specific	Cost of illness; patient	Prescription review	Current Index of Medical Specialities (CIMS) 1999, Indian Pharmaceutical Guide 1999	Only including costs of prescriptions/ drugs for patients with hypertension	Indian Rupees (INR)
Kapur 2007(41)	India	187 towns across India	5516 patients	mean age 53.7 (for DM type 2: 55.2 years)	1999	DM	Yes - not specific	Cost of illness; patient	Patient questionnaire survey	Self-report & responses of clinicians	Direct medical costs: est. total monthly expenditure on investigations, OP clinic, medicines, lab tests Direct non-medical costs: travel & misc. costs	Indian Rupee (INR)
Karan 2014(45)	India (national)	community (household survey) in India	74 000 households, 383 000 individuals	45% rural, male 50%	2004	CVD	Yes - CVD	Cost of illness; patient	National household survey	Self-reporting (from national household survey, India)	Direct medical costs: hospital care, outpatient, drugs Direct non-medical costs: travel	International Dollar (INT\$)
Khealani 2003(50)	Pakistan	Specialty hospital	443	mean age 58 years, Male 61%	1998-2001	CVD (acute stroke)	Yes - stroke	Cost of illness; patient	Case note review	Medical billing records	Direct medical costs: hospitalization, drug, diagnosis	Pakistan Rs / US\$

Khawaja 2007(54)	Pakistan (Karachi)	6 outpatient clinics in 3 different sites. (public, private and NGO)	345	Male 36.5%, 38% aged 51-60yrs, 36% aged 41-50yrs, 26% aged 20-40yrs	2006	DM	not specified	Cost of illness; patient	Patient questionnaire survey	Self-reported, The Pharmacy guide 2004, National Health Survey Pakistan (NHSP), Govt. of Pakistan	Direct medical costs: medicines, OP consultation, lab tests Direct non-medical costs: travel and food Indirect costs: loss of productivity	Pakistani Rupees
Kumar 2008(42)	India (Delhi)	High income wards of Delhi	819 subjects from 20,666 households	Male 51%, Mean age 54 years	09/2005-12/2005	DM type 2	No	Cost of illness, patient perspective	Household, cross-sectional survey	Self-reported	Direct medical costs - medicine use, lab tests, glucose testing and consultations.	Indian Rupees (INR)
Kumputa 2013(34)	India (Chennai)	Hospitalized pts in a Tertiary Hospital - Specialized diabetes care centre	368 (Stratified into 6 groups depending on complications)	Mean age 58 years, 70% urban	06/2008-12/2009	DM type 2 with complications	Yes	Cost of illness, patient perspective	cross-sectional patient questionnaire survey	Self-reported and hospital bills	Direct medical costs - current admission (medical consultations, lab, medicines, admission, surgery, investigations) and previous 2 years expenditure Direct non-medical costs - carer costs, transportation,	Indian Rupee (INR)
Kwatra 2013(51)	India (Punjab)	Stroke Unit and Neurology clinic of a tertiary referral centre	189	Mean age 58 years, male 68%	04/2009-10/2011	Stroke (CVD)	No	Cost of illness, societal perspective	Patient questionnaire survey, medical records review	Hospital bills, self-reported	Direct medical costs - admission, lab, radiology, investigations, drugs, nursing, appts, rehab Direct non-medical costs - travel, relocation, food, lodgings, changes to house etc. Indirect costs - productivity losses	Indian Rupees (INR)
Malhotra 2000(46)	India (Chandigarh)	Tertiary public sector hospital	336	Mean age 62 years, male 68%	6 month period in 1999	Unstable angina (CVD),	No	Cost of illness, patient perspective	Case note review & patient interviews	Pharmacy price list and self-reporting	Direct medical costs - (single admission) admission, prescription, coronary care unit, ward, interventions, investigations	US\$ and INR

Malhotra 2001(44)	India (Chandigarh)	Tertiary hospital outpatient department	1,076	Male 56%, mean age male: 51 yrs, female: 53 yrs	January-December 2000	Hypertension (CVD)	no	Cost of illness study, patient perspective	Medical records review and patient interview	Self-reported, hospital billing, pharmacy price list	Direct medical costs - Lab investigations, Drugs, Physician fees, ADRs (adverse drug reactions)	US\$ (Indian Rupees)
Marfati 2014(52)	India (Mumbai & Bangalore)	Tertiary Hospitals	400	Mean age 61 years, Male 62%	Jan 2010-Dec 2011	Stroke, with non-valvular atrial fibrillation	no	Cost of illness, societal	Patient questionnaire survey and case note review	Hospital billing records	Direct Medical Costs - Inpatient (hospitalisation, surgery, imaging, lab, medicines, rehab, ambulance) Outpatient (consultations, imaging, lab, medicines, rehab, nursing) Direct non-medical costs - Home modifications, transport Indirect costs - lost productivity	INR and US\$
Ramachandran 2007(35)	India	Various hospitals, clinics and rural areas of 7 states in India	556	56% urban, male 61%, mean age 56 years (urban) and 55 years (rural)	2005 (1 month)	DM type 2	no	Cost of illness, patient perspective	Patient questionnaire survey	Self-reported	Direct medical costs - medicines, lab, investigations, consultations, hospitalization, surgery	Indian Rupees (INR)
Rao 2011(47)	India (national)	Nationwide India (all 35 states)	Diabetes - 438 inpatients For CVD - 2,129 inpatients	CVD group - mean age 52 years, Male 54% DM group - mean age 55 years, Male 51%	01/2004-06/2004	CVD and diabetes mellitus	no	Cost of illness; patient perspective	Cross sectional household survey	Self-reported	Direct medical costs - doctors, medicines, lab, bed fee, nursing, physio, appliances, other (food, blood, oxygen, ambulance) Direct non-medical costs - transport, food and lodgings	Indian Rupee (INR)
Rayappa 1999(43)	India (Bangalore)	Various - hospitals and primary and community health centres (public)	611	Male 55%, illiterate 21%	1997	DM	no	Cost of illness, patient perspective	Patient questionnaire survey	Self-reported	Direct medical costs - Weekly expenditure on care, tests undertaken, hospitalisations Indirect costs - Working days lost and loss of personal/family income	Indian Rupees

		and private)										
Satyvani 2014(36)	India	a specialized diabetes care centre and a private hospital	209 (split into 4 groups depending on status of CKD)	Mean age 64 yrs. Male 58%, 60%, 76% and 57% in 4 groups	Aug 2008 - Jan 2010	DM type 2 with or without CKD	Yes only CKD	Cost of illness, patient perspective	Patient questionnaire survey and medical billing review	Self-reported and hospital bills	Direct medical costs - first admission (lab & consultations), medicines (monthly) and per hospitalization (surgery, bed fee, nursing), dialysis, total expenditure in past two years Direct non-medical costs - travel	Indian Rupees (INR)
Shastri 2015(49)	India (Karnataka)	Outpatient department of tertiary hospital	204	50% male, mean age 70 years	Not stated	CVD (DM as a comorbidity)	yes	cost of illness (medicines only), patient perspective	Case note review	www.cimsasia.com (online drug information system for Asia)	Direct medical cost - Cost of each drug in all the prescriptions for average cost of medications per day.	Indian Rupee
Shobhana 2000a(37)	India (Chennai)	One private hospital and one free Government hospital	596 (422 Private hospitals, 174 Government hospitals)	Priv hosp - 55% male, mean age 58 yrs. Govt hosp - 46% male, Mean age 55 yrs.	01/1998-06/1998	DM	No	Cost of illness, patient perspective	Patient questionnaire survey	Self-reported	Direct Medical costs - medicines, lab, doctors fee, hospitalisation, surgery Direct non-medical costs - travel	Indian Rupees (INR)
Shobhana 2000b(38)	India (Chennai)	Specialist hospital	270	Foot comp. group - 68% male, mean age 58 yrs, No foot comp. group - 50% male, mean age 55 yrs	Jan-June 1998	DM Type 2 only	Yes foot complications	Cost of illness study, patient perspective	Patient interviews	Self-reported	Direct medical costs - Doctors fees, specialist fees, surgery, hospitalisations, lab, medicines Direct non-medical costs - travel, footwear	Indian Rupees (INR)
Shrestha 2013(55)	Nepal	A public hospital, a private hospital and two poly clinics	227	Mean age 49yrs, Male 59%	07/2010-09/2010	DM	No	Cost of illness, patient perspective	Patient questionnaire survey	Self-reported	Direct Medical Costs - doctors fee, lab, medicine Direct Non-Medical Costs - travel, food and physical exercise Indirect cost - earnings	US \$

											lost due to clinic visit and having DM.	
Srivastava 2013(33)	India	National Indian surveys	n/a (modelling study)	n/a	National data sets - 2004, 1995/6, 2001/3	CVD	Not specifically	Macro-economic modelling study, societal perspective	Cross-sectional secondary data analysis	Self-reported (National household survey, India)	Direct medical costs - admission fee, drugs, lab, doctors fee Direct non-medical costs - travel, "other non-medical costs"	Indian Rupees (Rs)
Thakrar 2009(40)	India	diabetes specialty centre ( 100 beds) - location not stated	443 (269 without hypertension, 174 with hypertension)	Mean age 55 yrs, male 53%	10/2007-12/2007	DM (with or without hypertension)	Only hypertension	Cost of illness, patient perspective	Patient questionnaire survey	Self-reported	Direct medical costs - doctor's fees, medicines, lab, admission, investigations, misc. Direct non-medical costs - misc. (food, travel)	Indian Rupees (INR)
Thakrar 2010(39)	India	household, Chennai, India	718	53% male, mean age 56 yrs	08/2009-12/2009	DM with or without complications	Yes	Cost of illness, Societal perspective	Cross sectional Household survey	Self-reported	Direct medical costs - hospital service, consultation, lab, medicine Direct non-medical costs - food, transport Indirect costs - productivity losses Intangible cost - willingness to pay	Indian Rupees (INR)

Table 3 – Mean annual costs per patient of cardiovascular disease (CVD), Diabetes Mellitus (DM) and their complications (in US\$ 2015)

Ref.	Year	Condition	Country	Quality Score	Total costs	Direct medical costs	Direct non-medical costs	Indirect costs	Intangible costs
<b>Cardiovascular Disease</b>									
Karan 2014	2004	CVD	India (national)	78.1%		Mean annual costs - US\$ 563	Mean annual costs - US\$ 175.21	not included	not included
Srivastava 2013	2004	CVD	India	83.8%	The total cost of hospitalisation for CVDs in India in 2004 - US\$ 10.2 billion Modelled estimated costs - 2010 - US\$ 11.7 billion 2016 - US\$ 14.4 billion 2020 - US\$ 16.6 billion	Mean cost of hospitalisation for CVDs per person - 1995/96 - US\$ 1318 2004 - US\$ 1,523	Not disaggregated	not included	not included
Malhotra 2000	1999	CVD (angina - unstable)	India	75.8%	Mean total costs per hospitalisation episode - US\$ 677	Mean admission fee : US\$ 11 Cost of prescription per stay: US\$ 96; Cost of coronary care unit : US\$ 145; Cost of ward stay: US\$ 43; Cost of investigation: US\$ 154; Cost of interventions: US\$ 229	not included	not included	not included
Jhaj 2001	1999	CVD (Hypertension)	India (Chandigarh)	67.7%		Annual mean drug cost - US\$ 79	not included	not included	not included
Malhotra 2001	2000	CVD (Hypertension)	India	51.5%	Mean total annual cost - US\$ 386	Mean annual lab costs - US\$ 113 Mean annual drug costs: US\$ 231 Mean annual physician fees: US\$ 26	not included	not included	not included
<b>Cardiovascular Disease with Diabetes Mellitus</b>									
Shastri 2015	2014*	CVD (with or without DM)	India (Karnataka)	50.0%	Mean cost of prescription per day - All medications - US\$ 1.14 Cardiovascular diseases - US\$ 0.51 Diabetic medications - US\$ 0.21	Mean cost of prescription per day - All medications - US\$ 1.14 Cardiovascular diseases - US\$ 0.51 Diabetic medications - US\$ 0.21	not included	not included	not included
Rao 2011	2004	CVD and DM	India (national)	74.1%	Average costs per hospitalisation - US\$ 1,343 (CVD) and US\$ 646 (diabetes) Proportion of annual household income - 30% for CVD and 17% for diabetes	Not disaggregated from non-medical costs so unable to calculate.	Not disaggregated from direct medical costs so unable to calculate	not included	not included

Abegunde 2007	1950-2002**	CVD and DM	Pakistan, India, Bangladesh	83.3%	not included	not included	not included	Loss of GDP in 2015 - India - US\$ 1.96 billion Pakistan - US\$ 0.21 billion Bangladesh - US\$ 0.14 billion	not included
<b>Diabetes Mellitus (not specified)</b>									
Shrestha 2013	2010	DM	Nepal	76.6%	Mean total cost per outpatient visit - US\$ 14 Mean total cost per month - US\$ 44 Mean total cost per year - All pts - US\$ 483 Public sector - US\$ 219 Private sector - US\$ 606	Mean cost per visit: - US\$ 12  Mean cost per annum - All pts - US\$ 463 Public sector - US\$ 212 Private sector - US\$ 590	Mean cost per visit - US\$ 2.70  Mean annual cost - US\$ All pts - US\$21	Mean cost per visit: - US\$ 2.24  Mean cost per annum - Public sector - US\$ 9 Private sector - US\$ 27	not included
Akari 2013	2012	DM	India (Andhra Pradesh)	71.0%	Without complications - USD 31 With co-morbidities - USD 328	Without complication - USD 29 With co-morbidities - USD 303	Without complication - USD 0.37 With co-morbidities - USD 3.91	Without complications - USD 2.31 With co-morbidities - USD 21	not included
Chandra 2014	2011-12	DM	India (Pune)	45.3%		Average annual cost - US\$ 575	Average annual cost - US\$ 258	Average annual cost - US\$ 235	not included
Kapur 2007	1999**	DM	India	61.3%	Total estimated annual cost: US\$ 2,637	Mean total direct cost: - US\$ 948	Not clearly presented	Mean total indirect cost: US\$ 1,689	not included
Khowaja 2007	2006	DM	Pakistan (Karachi)	80.6%	Mean annual cost US\$ 1,048	Annual mean direct cost US\$ 951	Mean cost for travel - US\$ 10 Mean cost for food - US\$ 2.71	Mean lost productivity of pt - US\$ 9 Mean lost productivity of attendants - US\$ 17	not included
Rayappa 1999	1997	DM	India (Bangalore)	72.7%	Total annual costs of diabetes per person - Personal - US\$ 973 Family - US\$ 1,843 Society - US\$ 2,468	Average Annual Direct Cost for routine care (non-hospitalisation) - US\$ 882 Average Direct Cost per hospitalization - US\$ 1,471 Average annual cost of lab investigations and monitoring - US\$ 122	not included	Total annual indirect cost - US\$ 2,803	not included



Shobhana 2000a	1998	DM	India (Chennai)	77.9%	<p>Median total annual expenditure - Private hospital patients - US\$ 618 Public hospital patients - US\$ 34</p> <p>Estimated national costs for 20 million DM pts could be US\$ 12.4billion</p>	<p>Private hospital patients median spend - Medicine - US\$ 411 Lab tests - US\$ 49 Family doctor - US\$ 41 Specialist - US\$ 41 Hospitalisation - US\$ 685 Surgery - US\$ 1,233</p> <p>Public hospital patients median spend - Medicine - US\$ 101 Lab tests - US\$ 33 Family doctor - US\$ 16 Specialist - US\$ 75 Hospitalisation and surgery - Free care</p>	<p>Median transport costs for private hospital patients - US\$ 33</p> <p>Median transport costs for public hospital patients - US\$ 26</p>	not included	not included
<b>Diabetes Mellitus type 2</b>									
Ramachandran 2007	2005	DM type 2	India	65.2%	<p>Median total expenditure - Urban pts - US\$ 1,046 Rural pts - US\$ 655</p>	<p>Median total expenditure - Urban pts - US\$ 1,046 Rural pts - US\$ 655</p>	not included	not included	not included
Adiga Sachidananda 2010	2008	DM type 2	India (Karnataka)	58.1%	For hospitalised - US\$ 1,216	<p>Annual medicine costs - US\$ 648 to 1,963 Annual Consultation costs - US\$ 19 to 88</p>	not included	not included	not included
Hussain 2014	2013*	DM type 2	Pakistan (Karachi)	40.9%	Average cost - US\$ 213 per month (US\$ 2,551 annually)	not disaggregated	not disaggregated	not included	not included
Kumar 2008	2005	DM type 2	India (Delhi)	73.4%		Average costs ~ US\$ 628 per annum.	not included	not included	not included
Shobhana 2000b	1998	DM type 2	India (Chennai)	66.1%	<p>Group without foot complications - US\$ 599 Group with foot complications - US\$ 2,116</p> <p>Foot complications OP only - US\$ 986 Foot complications IP + OP - US\$ 2,316</p>	Not disaggregated from non-medical costs so unable to calculate.	<p>Group without foot complications - US\$ 38 Group with foot complications - US\$ 68</p> <p>Foot complications OP only - US\$ 58 Foot complications IP + OP - US\$ 68</p>	not included	not included
<b>Diabetes mellitus with complications</b>									

Clarke 2010	2001-6**	DM with complications	India (part of multi-country study)	75.0%		Major coronary event - US\$ 2,087 Major cerebrovascular event - US\$ 2,396 Heart Failure - US\$ 2,469 Peripheral vascular - US\$ 502 Nephropathy - US\$ 293  History of: Major coronary event - US\$ 131 Major cerebrovascular event - US\$ 122 Heart Failure - US\$ 205 Peripheral vascular - US\$ 168 Nephropathy: - US\$ 161	not included	not included	not included
Kumpatla 2013	2008-2009**	DM with complications (type 2)	India	69.1%	Total costs of hospital admission without complications - US\$ 362 Total costs of hospital admission with complications - US\$ 1,024 to 1,534  Estimated 2 year costs (no complications) - US\$ 2,420 Estimated 2 year costs (with complications) - US\$ 8,066 to 22,787	Not disaggregated from non-medical costs so unable to calculate.	transportation charges - US\$ 28 to 81 per admission	not included	not included
Ali 2008	1997-2004**	DM with foot ulcers	Pakistan	58.8%		Total Costs - Grade 1 foot ulcer = US\$ 246 Grade 2 = US\$ 3,406 Grade 3 = US\$ 4,466  Major amputation - US\$ 4,204 Minor amputation - US\$ 4,597	not included	not included	not included
Satyavani 2014	2008-2010**	DM (type 2) with or without CKD	India	67.2%	Total expenditure per hospitalisation - Transplantation group - US\$ 31,694 Dialysis group - US\$ 4,934 CKD group - US\$ 1,020 No complication group - US\$ 259  2 year total expenditure estimate - Transplantation group - US\$ 27,828 Dialysis group - US\$ 40,331 CKD group - US\$ 8,066 No complication group - US\$ 2,420	Not disaggregated from non-medical costs so unable to calculate.	The transportation charges per hospitalisation - Transplantation group -US\$ 262 Dialysis group - US\$ 281 CKD group - US\$ 50 No complication group - US\$ 24	not included	not included

Tharkar 2010	2009	DM with or without complications	India	89.1%	Median annual direct cost per patient -US\$ 2,048 Modelled annual national cost of diabetes to Indian population (range) - US\$ 99.2 billion to 148.2 billion).	not disaggregated from non-medical costs so unable to calculate.	Direct non-medical cost - Per hospitalisation - US\$ 202 Per OP attendance - US\$ 57	Median annual cost - US\$ 401	Patients' willingness to pay to stay well - Per month - US\$ 161 Per year - US\$ 1,936
Tharkar 2009	2007	DM with or without hypertension	India	59.4%	Mean total expenditure for hospital admissions over 2 year period - Non-hypertensive group = US\$ 2,603 Hypertensive group = US\$ 3,533	Median total cost for treatment of diabetes by hospitalization or inpatient procedure was - Non-hypertensive group - US\$ 1,734 Hypertensive group - US\$ 1,952  Average cost per routine out-patient check up - US\$ 288	Food and travel costs per hospitalisation episode - Non-hypertensive group = US\$ 399 Hypertensive group = US\$ 470	not included	not included
<b>Cardiovascular Disease - Stroke</b>									
Khealani 2003	1998-2001**	Stroke	Pakistan	66.1%		Total costs per stroke - US\$ 8,480	not included	not included	not included
Kwatra 2013	2009-2011**	Stroke	India	71.9%	The mean overall cost at 6 months - US\$ 5,966	Mean direct medical costs - US\$ 3,890 Inpatient care: US\$ 2,298 Outpatient care: US\$ 72 Inpatient rehabilitation: US\$ 73 Outpatient rehabilitation: US\$ 470 Total drugs charges: US\$ 1,411	Mean direct nonmedical costs - US\$ 357 (at 6 mths) Travel cost: US\$ 128 Other expenditures: US\$ 229	Mean indirect costs - US\$ 1,719 (at 6 mths) Patients: US\$ 1,088 Caregiver: US\$ 631	not included
Marfatia 2014	2010-11**	Stroke , with non-valvular atrial fibrillation	India	86.8%	Mean total costs per patient during first 12 months - US\$ 32,927 (median US\$ 29,706)	Index hospitalization – US\$ 15,366 Outpatient care - US\$ 13,085 GP visits US\$ 3,671 Rehabilitation services - US\$ 2,322 Laboratory visits - US\$ 261 Imaging visits - US\$ 875 Pharmacotherapy - US\$ 5,956 Nursing home/services - US\$ 2,083	Mean home modification costs US\$ 1,552	Mean costs for informal care (days of lost productivity) - US\$ 872	not included

\* No year of data collection reported, so year is assumed

\*\* Mid-year used to calculate conversion into 2015 US\$

Table 4 – Summary of annual costs for cardiovascular disease (CVD) and diabetes mellitus (DM) in South Asia (US\$ 2015)

<b>CVD</b>		
<b>Direct medical costs</b>	Hypertension outpatient care	US\$ 386
	Hypertension drugs	US\$ 79 - 231
	All CVD care per patient	US\$ 563
	All CVD drugs	US\$ 415
	CVD Hospitalisation costs	US\$ 677 - 1,523
	Per Stroke	US\$ 3,890 - 28,451
<b>Direct non-medical costs</b>	Per Stroke	US\$ 357 - 1,552
<b>Indirect costs</b>	Per Stroke	US\$ 872 – 1,719
	Loss of (national) productivity due to CVD	India US\$ 1.96 billion
		Pakistan US\$ 0.21 billion
Bangladesh US\$ 0.14 billion		
<b>Total societal costs</b>	Per stroke (First 12 months)	US\$ 5,966 - 32,927
<b>DM</b>		
<b>Direct medical costs</b>	Outpatient care	US\$ 463 - 951
	Including hospitalisation	US\$ 575 - 1216
	Minor complications	US\$ 246 – 502
	Major complications	US\$ 2,087 – 4,597
<b>Direct non-medical costs</b>	Outpatient care	US\$ 12 – 21
	Including hospitalisation	US\$ 258
	Complications per admission	US\$ 50 – 470
<b>Indirect costs</b>	All patients	US\$ 9 - 2,803
<b>Intangible costs</b>	Willingness to pay to stay well	US\$ 1,936

## Appendices

### Search Strategies for CVD / Diabetes Cost Studies in SE Asia

02-04-2015

#### EconPapers (RePec)

1. china\* or chinese or india or indian or indians or pakistan\* or bangladesh\* or afghan\* or maldiv\* or lanka or nepal\* or Bhutan
2. diabete\* or stroke or thrombosis or aneurysm or embolism or dvt or heart or cardiovascular or vascular or coronary or angina or myocardial or cardiac
3. 1 and 2 [in titles and keywords of working papers, articles, books and chapters]

#### Embase Classic+Embase <1947 to 2015 April 01>

- 1 (diabet\* or niddm or mody).tw. (641578)
- 2 exp \*diabetes mellitus/ (388539)
- 3 ((heart or cardiovascular or vascular) adj3 disease\*).tw. (380855)
- 4 ((myocardial or heart\*) adj5 infarc\*).tw. (219501)
- 5 (heart adj6 (disease\* or attack\*)).tw. (210921)
- 6 (coronary adj6 (disease\* or syndrome\*)).tw. (195411)
- 7 (angina or "transient ischaemic attack\*").tw. (67311)
- 8 (atherosclerosis or arteriosclerosis).tw. (136262)
- 9 "peripheral arterial disease".tw. (8682)
- 10 (stroke\* or (ischemia adj3 brain\*) or (infarc\* adj3 brain\*) or "intercranial haemorrhage\*" or "intercranial hemorrhage\*").tw. (250823)
- 11 (thrombosis or occulsion\* or thromboses or aneurysm\* or embolism\*).tw. (321198)
- 12 DVT.tw. (11938)
- 13 ("atheromatous plaque" or atheromata\*).tw. (1581)

- 14 \*heart disease/ or \*cardiovascular disease/ or \*heart failure/ or exp \*heart arrest/ (218801)
- 15 \*vascular disease/ or exp \*peripheral vascular disease/ or exp \*portal hypertension/ or exp \*thromboembolism/ (970367)
- 16 \*ischemic colitis/ (1405)
- 17 exp \*ischemic heart disease/ or \*heart muscle ischemia/ (293815)
- 18 exp \*cardiomegaly/ (23258)
- 19 exp \*diabetic angiopathy/ (6269)
- 20 exp \*artery occlusion/ (42515)
- 21 \*prehypertension/ or \*hypertension/ (193494)
- 22 \*reperfusion injury/ (21122)
- 23 exp \*retina vein occlusion/ (3792)
- 24 \*cerebrovascular accident/ (47933)
- 25 or/1-24 [Diabetes or CVD terms] (2569474)
- 26 China/ (110932)
- 27 India/ (101303)
- 28 Pakistan/ (17294)
- 29 Bangladesh/ (10228)
- 30 Afghanistan/ (3940)
- 31 nepal/ (6798)
- 32 Sri Lanka/ (5814)
- 33 Bhutan/ (365)
- 34 maldives/ (143)
- 35 (china or chinese or india or indian or pakistan\* or bangladesh\*).ti,ab,in. (1826291)
- 36 (afghanistan\* or maldives or bhutan\* or nepal\* or "sri lanka\*").ti,ab,in. (25293)
- 37 or/26-36 [SE Asian World Bank LMICs] (1886276)
- 38 \*budget/ (4899)

- 39 budget impact stud\*.tw. (9)
- 40 (cost\* or economic\* or expenditure\*).ti. (161426)
- 41 "cost of illness"/ (14986)
- 42 exp \*economic evaluation/ (38228)
- 43 (expenditure\* adj5 (healthcare or medical or treatment)).tw. (5796)
- 44 (economic\* adj2 (analysis or burden or evaluation\* or consequence\*)).ab. (21004)
- 45 (cost\* adj2 (illness or evaluat\* or analy\* or compar\* or efficienc\* or estimate\*)).ab. (54565)
- 46 or/38-45 (216687)
- 47 25 and 37 and 46 (1123)
- 48 exp animals/ not (exp animals/ and exp humans/) (4681580)
- 49 exp nonhuman/ not (exp nonhuman/ and exp human/) (3548685)
- 50 exp experimental animal/ (465642)
- 51 exp veterinary medicine/ (34563)
- 52 animal experiment/ (1843743)
- 53 ((energy or oxygen\* or metaboli\*) adj3 (expenditure\* or cost\*)).tw. (29818)
- 54 or/48-53 (6293730)
- 55 47 not 54 (1035)

### **Global Health <1973 to 2015 Week 12>**

- 1 (diabet\* or niddm or mody).tw. (84109)
- 2 diabetes/ or diabetes mellitus/ (50886)
- 3 exp cardiovascular diseases/ (78197)
- 4 ((heart or cardiovascular or vascular) adj3 disease\*).tw. (75247)
- 5 ((myocardial or heart\*) adj5 infarc\*).tw. (8505)
- 6 (heart adj6 (disease\* or attack\*)).tw. (40986)
- 7 (coronary adj6 (disease\* or syndrome\*)).tw. (31595)

- 8 (angina or "transient ischaemic attack\*").tw. (1975)
- 9 (atherosclerosis or arteriosclerosis).tw. (16605)
- 10 "peripheral arterial disease".tw. (510)
- 11 (stroke\* or (ischemia adj3 brain\*) or (infarc\* adj3 brain\*) or "intercranial haemorrhage\*" or "intercranial hemorrhage\*").tw. (12558)
- 12 (thrombosis or occlusion\* or thromboses or aneurysm\* or embolism\*).tw. (7506)
- 13 DVT.tw. (262)
- 14 ("atheromatous plaque" or atheromata\*).tw. (99)
- 15 or/1-14 [CVD or Diabetes] (170221)
- 16 (china or chinese or india or indian or pakistan\* or bangladesh\*).ti,ab,in. (387962)
- 17 (afghanistan\* or maldives or bhutan\* or nepal\* or "sri lanka\*").ti,ab,in. (10166)
- 18 exp bangladesh/ (7253)
- 19 exp India/ (72195)
- 20 exp china/ (109156)
- 21 exp Pakistan/ (9714)
- 22 afghanistan/ (1121)
- 23 maldives/ (88)
- 24 bhutan/ (227)
- 25 nepal/ (3979)
- 26 sri lanka/ (3152)
- 27 or/16-26 [SE Asian World Bank LMICs] (405865)
- 28 economic evaluation/ (526)
- 29 health care costs/ (7166)
- 30 budgets/ (233)
- 31 budget impact stud\*.tw. (1)
- 32 (cost\* or economic\* or expenditure\*).ti. (23122)



- 33 (cost\* adj2 (illness or evaluat\* or analy\* or compar\* or efficienc\* or estimate\*)).ab. (7533)
- 34 (economic\* adj2 (analysis or burden or evaluation\* or consequence\*)).ab. (3480)
- 35 (expenditure\* adj5 (healthcare or medical or treatment)).ab. (945)
- 36 or/28-35 [Cost Studies] (31990)
- 37 15 and 27 and 36 (267)
- 38 exp animals/ not (man/ or women/) (524796)
- 39 ((energy or oxygen\* or metaboli\*) adj3 (expenditure\* or cost\*)).tw. (10100)
- 40 38 or 39 (533179)
- 41 37 not 40 (233)

### **Ovid MEDLINE(R) <1946 to March Week 5 2015>**

- 1 exp Diabetes Mellitus/ (322574)
- 2 (diabet\* or niddm or mody).tw. (397491)
- 3 ((heart or cardiovascular or vascular) adj3 disease\*).tw. (247187)
- 4 cardiovascular diseases/ or heart diseases/ or cardiac output, high/ or cardiac output, low/ or cardiomegaly/ or heart aneurysm/ or heart arrest/ or heart failure/ or myocardial ischemia/ or vascular diseases/ or arterial occlusive diseases/ or cerebrovascular disorders/ or colitis, ischemic/ or diabetic angiopathies/ or "embolism and thrombosis"/ or hypertension/ or optic neuropathy, ischemic/ or peripheral vascular diseases/ or prehypertension/ or reperfusion injury/ or retinal vein occlusion/ (622120)
- 5 ((myocardial or heart\*) adj5 infarc\*).tw. (145464)
- 6 (heart adj6 (disease\* or attack\*)).tw. (137474)
- 7 (coronary adj6 (disease\* or syndrome\*)).tw. (126119)
- 8 (angina or "transient ischaemic attack\*").tw. (44698)
- 9 exp Atherosclerosis/ (23981)
- 10 (atherosclerosis or arteriosclerosis).tw. (88321)
- 11 "peripheral arterial disease".tw. (5429)

- 12 (stroke\* or (ischemia adj3 brain\*) or (infarc\* adj3 brain\*) or "intercranial haemorrhage\*" or "intercranial hemorrhage\*").tw. (153299)
- 13 thrombosis/ or coronary thrombosis/ or exp thromboembolism/ or exp venous thrombosis/ (144247)
- 14 (thrombosis or occulsion\* or thromboses or aneurysm\* or embolism\*).tw. (207687)
- 15 DVT.tw. (6302)
- 16 ("atheromatous plaque" or atheromata\*).tw. (1018)
- 17 Stroke/ (62926)
- 18 or/1-17 [Diabetes or CVD] (1648865)
- 19 exp china/ or bangladesh/ or exp india/ or pakistan/ (194127)
- 20 (china or chinese or india or indian or pakistan\* or bangladesh\*).ti,ab,in. (910571)
- 21 (afghanistan\* or maldives or bhutan\* or nepal\* or "sri lanka\*").ti,ab,in. (15461)
- 22 afghanistan/ (2341)
- 23 Nepal/ (5096)
- 24 Sri Lanka/ (4203)
- 25 Bhutan/ (211)
- 26 or/19-25 [SE Asian World Bank LMIC Countries] (968791)
- 27 exp "Costs and Cost Analysis"/ (185787)
- 28 exp budgets/ (12272)
- 29 budget impact stud\*.tw. (4)
- 30 (cost\* or economic\* or expenditure\*).ti. (113918)
- 31 (cost\* adj2 (illness or evaluat\* or analy\* or compar\* or efficienc\* or estimate\*)).ab. (33530)
- 32 (economic\* adj2 (analysis or burden or evaluation\* or consequence\*)).ab. (12628)
- 33 (expenditure\* adj5 (healthcare or medical or treatment)).ab. (3644)
- 34 or/27-33 [Cost Studies] (255440)
- 35 18 and 26 and 34 (592)

- 36 exp animals/ not (exp animals/ and exp humans/) (4003797)
- 37 exp Veterinary Medicine/ (21693)
- 38 exp Animal Experimentation/ (6539)
- 39 ((energy or oxygen\* or metaboli\*) adj3 (expenditure\* or cost\*)).tw. (21844)
- 40 or/36-39 (4036443)
- 41 35 not 40 [CVD Diabetes Costs and Countries] (558)

### **Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <April 01, 2015>**

- 1 (diabet\* or niddm or mody).tw. (36485)
- 2 ((heart or cardiovascular or vascular) adj3 disease\*).tw. (20289)
- 3 ((myocardial or heart\*) adj5 infarc\*).tw. (8129)
- 4 (heart adj6 (disease\* or attack\*)).tw. (9106)
- 5 (coronary adj6 (disease\* or syndrome\*)).tw. (8857)
- 6 (angina or "transient ischaemic attack\*").tw. (2064)
- 7 (atherosclerosis or arteriosclerosis).tw. (5830)
- 8 "peripheral arterial disease".tw. (495)
- 9 (stroke\* or (ischemia adj3 brain\*) or (infarc\* adj3 brain\*) or "intercranial haemorrhage\*" or "intercranial hemorrhage\*").tw. (15126)
- 10 (thrombosis or occulsion\* or thromboses or aneurysm\* or embolism\*).tw. (14982)
- 11 DVT.tw. (610)
- 12 ("atheromatous plaque" or atheromata\*).tw. (49)
- 13 budget impact stud\*.tw. (2)
- 14 (cost\* or economic\* or expenditure\*).ti. (10353)
- 15 (cost\* adj2 (illness illness or evaluat\* or analy\* or compar\* or efficienc\* or estimate\*)).ab. (3765)
- 16 (economic\* adj2 (analysis or burden or evaluation\* or consequence\*)).ab. (1911)

- 17 (expenditure\* adj5 (healthcare or medical or treatment)).ab. (443)
- 18 or/13-17 [Cost Studies] (13343)
- 19 (china or chinese or india or indian or pakistan\* or bangladesh\*).ti,ab,in. (249078)
- 20 (afghanistan\* or maldives or bhutan\* or nepal\* or "sri lanka\*").ti,ab,in. (2578)
- 21 19 or 20 [SE Asian World Bank LMICs] (251129)
- 22 or/1-12 [CVD or Diabetes] (89343)
- 23 18 and 21 and 22 (93)

### **NHS Economic Evaluation Database : Issue 1 of 4, January 2015 (Wiley)**

- #1 (diabet\* or niddm or mody):ti,ab
- #2 ((heart or cardiovascular or vascular) near/3 disease\*):ti,ab
- #3 ((myocardial or heart\*) near/5 infarc\*):ti,ab
- #4 (heart near/6 (disease\* or attack\*)):ti,ab
- #5 (coronary near/6 (disease\* or syndrome\*)):ti,ab
- #6 (angina or "transient ischaemic attack\*"):ti,ab
- #7 (atherosclerosis or arteriosclerosis):ti,ab
- #8 "peripheral arterial disease":ti,ab
- #9 (stroke\* or (ischemia near/3 brain\*) or (infarc\* near/3 brain\*) or "intercranial haemorrhage\*" or "intercranial hemorrhage\*"):ti,ab
- #10 (thrombosis or occulsion\* or thromboses or aneurysm\* or embolism\*):ti,ab
- #11 DVT:ti,ab
- #12 ("atheromatous plaque" or atheromata\*):ti,ab
- #13 MeSH descriptor: [Diabetes Mellitus] explode all trees
- #14 MeSH descriptor: [Cardiovascular Diseases] explode all trees
- #15 MeSH descriptor: [Stroke] explode all trees
- #16 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15

- #17 MeSH descriptor: [China] explode all trees
- #18 MeSH descriptor: [India] explode all trees
- #19 MeSH descriptor: [Pakistan] explode all trees
- #20 MeSH descriptor: [Bangladesh] explode all trees
- #21 MeSH descriptor: [Afghanistan] this term only
- #22 MeSH descriptor: [Sri Lanka] this term only
- #23 MeSH descriptor: [Nepal] this term only
- #24 MeSH descriptor: [Bhutan] this term only
- #25 (china or Chinese or india or indian or Indians or Pakistan\* or Bangladesh\*):ti,ab
- #26 (afghan\* or Bhutan or Maldives or "sri lanka" or Nepal\*):ti,ab
- #27 #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26
- #28 #16 and #27

## **WHOLIS World Health Organization Library & Information Networks for Knowledge Database**

Searches in 'words and phrases'

1. diabetes or diabetic or heart or cardiac or stroke or thrombosis or aneurysm or embolism or dvt or cardiovascular or vascular or coronary or angina or myocardial
2. cost or economic or expenditure or budget
3. india or indians or china or chinese or pakistan or pakistani or bangladesh or Bangladeshi or nepal or nepalese or bhutan or maldives or afghanistan or afghanistani or lanka
4. 1 and 2 and 3

## DATA EXTRACTION FORM

<b>Reviewer:</b>	
<b>Date of Review</b>	
<b>Authors:</b>	
<b>Title</b>	
<b>Reference:</b>	
<b>Year:</b>	
<b>Country:</b>	
<b>Language</b>	
<b>Meeting exclusion criteria</b> Give yes/no answer, if yes give details about which exclusion criteria is met:	Yes/ No <b>Exclusion criteria</b> <ul style="list-style-type: none"> <li>- no full text publication was available, and Conference abstracts only available</li> <li>- Written in language other than English, Chinese, Hindi, Urdu or Bengali</li> <li>- Costs not relating to costs of usual care in the setting at the time, or only to costs of an intervention</li> </ul>
<b>Aim of study:</b>	
<b>Condition</b> What condition does the study address and how was it defined?	
<b>Patient population</b>	
<b>Setting:</b>	
<b>Year of data collection</b>	
<b>Sample Size</b>	
<b>Recruitment process</b>	
<b>Exclusion criteria:</b>	
<b>Population demographics assessed</b>	
<b>Economic study design</b>	
<b>Study Type</b> Is the study type clearly specified, what study type is it reported as, and is	

this consistent with the methodology presented	
<b>Perspective of the analysis:</b> 1) patient only; 2) societal 3) health service	
<b>The Analysis process used</b> how was the data analysis performed? Including projections or only timeframe of data collection?	
<b>Economic Modelling:</b> Was modelling performed? if yes, what models were used (description) and what information informed the model?	
<b>Source of cost data:</b>	
<b>Primary outcome measures</b> (if applicable) What measures were used?	
<b>Costs included (including sources)</b>	
<b>Direct medical costs</b> This includes all expenditures relating to medical care (Hospital admissions, Investigations, treatment (including medication), out-patient visits etc.)	
<b>Direct non-medical costs:</b> This includes all expenditure incurred as a result of the disease or condition that are not medical expenditures (travel costs, subsistence costs, accommodation costs, costs for support or	

changes to home environment etc.)	
<b>Indirect costs:</b> Indirect cost are not direct expenditures, but costs incurred as a result of the illness (like time off work, loss of income, opportunity cost, Sickness, disability, premature retirement or premature mortality etc)	
<b>Intangible costs:</b> By definition, intangible costs are costs that are difficult to capture. This includes cost to society, like absteentism, pain, anxiety, inconvenience, loss of quality of life etc)	
<b>Excluded costs:</b> Give information as to costs that are clearly mentioned as excluded, or that you can see that have not been included	
<b>Source of resource use and unit costs:</b>	
<b>Currency:</b> <b>Price year:</b> Also include what methods were used for conversion of prices if relevant.	
<b>Discounting (costs/benefits)</b> ( Was discounting done I time horizon of the study > 1year, and if yes what rate was applied and were they applied to costs and / or benefits):	
<b>Sensitivity analysis:</b> (was a sensitivity analysis performed, was parameters were	



modelled, and did what was the outcome of it?)	
<b>Cost results</b>	
<b>Direct Medical:</b>	
<b>Direct non-medical:</b>	
<b>Indirect</b>	
<b>Intangible</b>	
<b>Cost for patient</b>	
<b>Cost for health care service</b>	
<b>Costs for society:</b>	
<b>Other costs:</b>	
<b>Authors' conclusions</b>	
<b>Summary Findings:</b>	
<b>Comments – limitations:</b>	

### Quality Checklist :

	yes	no	partial	not clear	NA	comment
Item						
study question stated and well defined?						
well defined aim of the study?						
Is the study population described ?						
Is the study population representative of the source population?						
Is the process of identifying and recruiting subjects clear and appropriate?						
Is the study setting and location clearly defined?						
Was the disease adequately defined?						
Has the study perspective been clearly defined?						
Is the time horizon clearly specified?						
The form of economic evaluation used is stated						
The choice of form of economic evaluation is justified in relation to the questions addressed.						

Was an appropriate method of quantification used?						
Was the resource quantification well executed?						
<b>MEASUREMENT OF RESOURCES DATA</b>						
Are the sources used to collect resource utilisation data reported clearly (e.g. clinical trials, administrative databases, clinical databases, medical records and published literature)?						
Are the resource quantities reported independently from the costs, so that assessment of the measurement method is facilitated?						
Are any assumptions in the measurement of resources explicitly reported and justified?						
If an expert was consulted to estimate some of the resources, are the methods used described?						
If this is a trial: were the resource estimates collected prospectively alongside effectiveness data, utilising the robust infrastructure established for the trial?						
If the resources utilised were identified through a literature review are details of the review process provided and robust?						
<b>VALUATION OF RESOURCES DATA</b>						
Are all the sources used to obtain unit costs reported and relevant for the specific study setting?						
If prices were used instead of costs and cost-to-charge ratios calculated, do these reflect the true opportunity costs of the strategies compared?						
Did the analysis address the study question?						
Was a range of estimates presented?						
Were the main uncertainties identified?						
Was a sensitivity analysis performed? (and variables varied justified)						
Discount rate is stated and justified? (If the time horizon for estimating costs was longer than one year was discounting performed in order to reflect time preferences?)						
Reports currency, price date and conversion?						

Are all costs adjusted to a specific price year so that the effects of inflation are removed from the cost estimation?						
Details of model used given?						
Was adequate documentation and justification given for cost components, data sources, assumptions and methods?						
Were all included costs clearly described and all relevant costs included?						
Were the costs addressed related to usual practice in that country/ setting?						
Was uncertainty around estimations and its implications as well as limitations, discussed?						
Were the results presented at the appropriate level of detail to answer the study question?						
Is the answer to the study question given?						
Conclusion follow from the data reported?						
Are the study results internally valid (i.e unbiased)? How well did study minimise bias? Any significant flaws in study design?						
Are the findings generalizable to the source population (i.e externally valid)? Sufficient details given to determine if findings generalizable to source population?						
summary score						
Score						
If yes is >70% good quality						
If yes is >50% fair quality						
If yes is <49% then weak quality						