Annex 1A. Costing the Essential Package for Cardiovascular, Respiratory, and Related Disorders Notes

Supplementary material for: Prabhakaran, D, S Anand, DA Watkins, TA Gaziano, Y Wu and others. 2017. "Cardiovascular, Respiratory, and Related Disorders: Key Messages on Essential Interventions to Address its Burden in Low-and Middle-Income Countries." In *Cardiovascular, Respiratory, and Related Disorders* edited by D Prabhakaran, S Anand, TA Gaziano, J-C Mbanya, Y Wu, and R Nugent. Volume 5 of *Disease Control Priorities, third edition.* Washington, DC: World Bank.

Annex prepared by David Watkins and Jinyuan Qi

BACKGROUND

Estimating the cost of a package of interventions and policies for the conditions and risk factors covered in this Volume is challenging because, to our knowledge, no widely-applied costing tools are available for cardiovascular and related disorders (CVRDs) aside from work conducted by WHO-CHOICE, which unfortunately does not cover all of the conditions and interventions covered in this Volume.[1] We reviewed and discussed the methods, data sources, and limitations of previous efforts to estimate the cost of essential packages of care. Described below is an approach that has been deemed to be most feasible for costing a package of services for CVRDs.

METHODS

Costing approach used in this analysis

We used a "comparative statics" approach to estimate the potential cost of the CVRD Essential Package (EP). In a comparative statics analysis, one exogenous variable/parameter in a model is changed and the quantity of interest, conditional on changes in all other endogeneous variables/parameters in the model, is re-estimated.[2] Our costing question was posed as follows:

> *Given current demographic and epidemiological patterns and intervention costs, how much more would a typical low- or lower middle-income country be spending annually in the year 2030 if it had already achieved upper middle-income country levels of coverage of the CVRD EP interventions?*

The rationale for framing the costing question in this way was twofold. First, for *DCP3,* we adopt the "progressive universalist" approach to healthcare finance as outlined in the Global Health 2035 report and endorsed by the recent "Making Fair Choices" WHO consultation.[3,4] Progressive universalism advocates for 100% prepayment of interventions – i.e., that government assumes 100% of the unit cost of the intervention and finances care through general revenues rather than user fees. It advocates for full population coverage for a specified (albeit limited) list of interventions. So we were interested in the additional (incremental) cost to government arising from the additional proportion of patients covered under a "universal" scheme. This universal health coverage (UHC) orientation also situates our costs within the Sustainable Development Goal (SDG) 3 target of UHC. Yet we recognize that achieving "universal" coverage (i.e., 95-100% of the population) is unlikely to be feasible for low- or lower middle-income countries by

the year 2030, so in costing this package we set a more realistic target: "convergence" to upper middle-income country coverage levels.[3]

Second – pragmatically – it is infeasible to attempt to produce a global "price tag" for CVRD as has been done in previous maternal-child health and infectious diseases "investment cases."[5,6] As described above, there are simply not adequate data nor accepted methods for doing this sort of costing for CVRD. We do note that our approach assumes that all variables, including unit costs, are at equilibrium and/or at long-run averages, the exception being population coverage rates, which are exogenous. This assumption makes the cost estimation feasible using available data. Yet it does not explicitly address potential additional health system investments over and above the average rate of depreciation of capital and labor which are factored into these long-run average costs.

We define ex ante the proportion of unit costs to be prepaid (100%) and the list of interventions to be publicly financed (i.e., the CVRD EP). We explore the difference in cost that results from increasing population coverage from current levels to "universal" levels. This approach is especially relevant for CVRD interventions, which currently have very low coverage rates in low- and lower-middle income countries as compared to, e.g., infectious disease interventions and maternal and child health interventions. The incremental cost that we estimate, then, is the increase in cost from the government's perspective that is due to the increase in the proportion of the population covered by the EP.

A simple equation for the incremental cost K_1 of the EP, containing *n* interventions is

$$K_1 = \sum_{i=1}^{n} pop_i \times \Delta cov_i \times cost_i$$

where pop_i is a number of individuals per 100,000 population in need of intervention i, Δcov_i is the difference in the proportion of individuals covered ex post minus ex ante (e.g., Δcov_i = 0.8 if current coverage is 10% and target coverage is 90%), and $cost_i$ is the yearly per-patient cost of the intervention (ideally incorporating both recurrent costs and annualized capital costs). Again, equilibrium is assumed ex ante and ex post, and Δcov_i is the exogenous parameter.

However the total health system cost of the package might be higher or lower than what is estimated by microcosting studies ($cost_i$) due to administrative, logistical, and other health system strengthening costs. The incremental cost K_2 of the entire package, factoring in potential health system costs, can then be approximated as

$$K_2 = K_1 + A(K_1)$$

where $A(K_1)$ is a function of pop_i, Δcov_i, and $cost_i$. Previous large-scale costing efforts have used a scalar estimate of $A(K_1)$ of 0.5 based on empirical relationships between intervention unit costs and health system strengthening costs.[7,8] This approach to estimating costs assumes 1) that the microcosting studies used to calculate $cost_i$ reasonably reflect the economic costs from the health system perspective, 2) that they approximate long-run average costs, and 3) that the health system requires additional investment above and beyond what is costed out in any given study.

Epidemiological inputs and assumptions

The choice of pop_i and Δcov_i drives the total cost estimates in this analysis. To characterize pop_i for "typical" low-income (LI) and lower middle income (LMI) country scenarios, we aggregated previously published epidemiological and demographic estimates into LI and LMI country groups, then we divided our estimates for LI and LMI by relevant population sizes to arrive at epidemiological parameters per 100,000 population in either income group.

Most estimates of prevalence as well as population structure were taken from the Global Burden of Disease 2013 Study.[9] However we calculated peripheral vascular disease prevalence by extrapolating from the GBD 2010 estimates and breaking down LMIC costs into LI and LMI country groups based on relative proportion of the populations 70 years or older.[10]

We took crude prevalence estimates of smoking and hypertension from the WHO Global Health Observatory.[11] In some instances, we used country-specific data from Niger (a representative LI country) or India (a representative LMI country) when aggregate LI or LMI estimates were unavailable. These include school attendance rates and incidence of live births, both of which were taken from the UN database,[12] as well as ischemic stroke and chronic kidney disease prevalence, both of which were taken from GBD 2013.

To calculate rates of acute CVD events, we estimated disease incidence as the ratio of disease prevalence to disease duration. Estimates of duration are sparse in LMICs, so we took these from the 1999 Australia Burden of Disease Study.[13] Table 1A.1 breaks down the relevant epidemiological parameters by income group.

Table 1A.1 Epidemiological inputs for EP costing

		LI country	*LMI country*
Condition	*Parameter type*	*Rate*	*Rate*
Elevated systolic blood pressure	prevalence	27600	25200
Tobacco use (not including second-hand smoking)	prevalence	10500	12400
Pregnancy	incidence	4970	2144
Type 2 diabetes mellitus (not specified as Type 2)	prevalence	2133	4606
Chronic obstructive pulmonary disease	prevalence	2332	1914
Acute exacerbation of chronic obstructive pulmonary disease	incidence	159	130
Asthma	prevalence	2135	2684
Chronic ischemic heart disease	prevalence	629	768
Acute myocardial infarction	incidence	131	160
Chronic ischemic stroke	prevalence	37	127
Acute ischemic stroke	incidence	18	60
Chronic peripheral vascular disease	prevalence	2	2
Acute peripheral vascular disease	incidence	<1	<1
Chronic heart failure	prevalence	468	586

Acute heart failure	incidence	360	451
Chronic kidney disease	prevalence	956	647

Note: All rates are per 100,000 population. Heart failure estimates are for cardiac etiologies of heart failure only.

To characterize Δcov_i, we need to know current coverage rates of interventions and select a feasible target coverage rate (the difference between the two being the incremental coverage rate). Unfortunately, indicators of coverage of NCD services are not currently included among the WHO's list of indicators. However, Khatib and colleagues recently reported the availability of selected cardiovascular medications in a variety of countries in all four World Bank income groups.[14] The average coverage rates of these medications are shown in Table 1A.2, and we use these estimates as a proxy for coverage of general CVRD services.

Table 1A.2 Coverage rates of selected cardiovascular medications

	Urban	*Rural*	*Weighted average*
High-income	95%	90%	94%
Upper middle-income	80%	73%	77%
Lower middle-income	62%	37%	47%
Low-income	25%	3%	10%

Note: Data from Khatib and colleagues, Lancet 2016. Weighted average calculated by DCP3 authors.

There are several potential choices of target and incremental coverage rates. As described previously, we chose upper middle-income country coverage rate (77%) as the reference for lower middle-income and low-income countries, reflecting the sort of coverage that might be achievable during the Sustainable Development Goals period.[15] Incremental coverage for low- and lower middle-income country EP costs is about 67% and 30%, respectively.

Intervention cost inputs and assumptions

The choice of $cost_i$ for each intervention is slightly more challenging, since there are limited cost data for each EP intervention. We drew heavily on cost analyses (CA) and cost-effectiveness analyses (CEA) for CVRD that were reviewed for *DCP3*.[16] We selected the highest-quality studies that provided interventions most like the EP interventions. We preferentially took studies from low-income and lower middle-income countries, although we had to rely on upper middle-income country studies in many cases. For a few interventions, there were no relevant CA or CEA included in the *DCP3* review, so we searched the literature for cost estimates.

When necessary, we standardized the cost estimates to annual per-patient costs (in the case of interventions for chronic, prevalent conditions such as hypertension or secondary prevention of ischemic heart disease) or costs per patient-episode (in the case of interventions for acute, one-off interventions such as acute pharyngitis or acute myocardial infarction).

Cost estimates used for EP interventions

This section provides details on which study was used for each EP intervention and any additional calculations or assumptions that were required.

Tax tobacco products. We used costs from a CEA of tobacco control interventions in Vietnam.[17] The cost components included planning, human resources, program supplies, media strategy, and administrative overhead. We did not include potential revenue generated (i.e., negative costs) in our estimate of the program cost. We divided the total costs associated with increased taxation by the population of Vietnam during the study period to estimate cost per capita.

Tax sugar-sweetened beverages. To our knowledge, no studies have been published on the cost of this sort of intervention. We assumed the same cost as the tobacco tax intervention above.[17]

Improve built environment to encourage physical activity. We used costs from a benefit-cost analysis of an intervention in four urban areas to promote bicycling.[18] Specifically, we used average costs from two areas in Colombia that were thought to be most representative of typical LMIC settings. We divided total annual costs associated with this intervention by the population in the two cities represented to estimate cost per capita.

School based programs to improve nutrition and encourage physical activity. We used costs from a CEA of a multicenter trial of nutrition and physical education in China.[19] We extracted costs per student in different centers and scaled them up to the national level using national consumption and wage data from National Bureau of Statistics of China (2010). To estimate the cost of this intervention in our package, we multiplied this cost per child by the number of children of school-going age and then by the school attendance rate.

Regulation on advertising and labeling tobacco products. These costs were taken from the aforementioned CEA in Vietnam.[17]

Nutritional supplementation for women of reproductive age. There is some discretion as to the components of nutritional supplementation according to the goals of supplementation and the underlying epidemiology, e.g., prevalence of anemia. We did not identify any studies related to cardiovascular protection through nutritional supplementation in this group, so we used costs from a CEA of micronutrient supplementation in Vietnam as a proxy.[20] We multiplied the annual costs per woman by the population of reproductive age (females aged 15-49).

Regulations to reduce salt in manufactured food products. We used costs from a CEA of salt reduction policies in Eastern Mediterranean countries.[21] In particular, we used public costs of regulation, taking the average cost in Turkey and Tunisia weighted by the population size, then divided by the total population to estimate cost per capita.

Mass media health promotion targeted towards specific unhealthy foods. The aforementioned CEA of salt reduction assessed the cost of mass media health promotion around discretionary salt use.[21] We assumed this to be similar to the cost of a media campaign around other unhealthy foods. The same procedure as above for estimating cost per capita was used for this intervention.

Ban trans fat. We used costs from a CEA of a trans fat ban in Argentina.[22] We took the annual surveillance and monitoring costs borne by the Ministry of Health and divided them by the population size to estimate cost per capita.

Promotion of healthy fats in the diet. No study directly assessed the cost of this intervention. We assumed that a reasonable proxy would be the cost of a mass media health promotion campaign on unhealthy foods, so this cost was the same as the "unhealthy foods" cost above.

Use of CHWs for screening CVRD using non-lab based tools for overall CVD risk. We used costs from a CEA of CHWs screening for lipid disorders in three countries.[23] We took the costs of the paper-based screening intervention in South Africa, which we judged to be the most representative cost for typical LMIC settings. To estimate the total number requiring screening in a given year (total cost), we assumed that all individuals over 30 in the population would be screened for one CVRD yearly so multiplied this cost per case screened by the population size and then by proportion over 30.

Use of community health workers for encouraging adherence to medications. We used costs from a CEA of CHWs who assisted with hypertension medication adherence in South Africa.[24] We assumed that the crude prevalence of hypertension was a reasonable approximation of the proportion of the population in need of adherence support. To estimate the total cost, we multiplied the unit cost by the number of people with hypertension.

Tobacco cessation counseling, and use of nicotine replacement therapy in certain circumstances. We used costs from a CEA of personalized tobacco cessation treatment in Vietnam.[17] We calculated the weighted average cost per smoker of brief advice (80%) and nicotine replacement (patch or gum, 10% each).

Opportunistic screening for hypertension for all adults. There were no studies in the *DCP3* systematic reviews that addressed this intervention, so we took costs from a WHO CA of various NCD interventions.[25] Specifically, we used the cost of primary care screening for CVD in adults, and we applied this to the number of adults over 30 years in our populations, adjusting by typical healthcare utilization rates as evidenced by recent Demographic and Health Survey data (50% for Niger, a representative LI country, and 70% for India, a representative LMI country).

Screening for diabetes in all high-risk adults including pregnant women. We used costs from two different studies. The first study looked at population-based diabetes screening in Brazilian adults.[26] We divided the total cost of the screening program and the number of individuals screened to estimate the cost per case screened. We then multiplied this by the number of adults over 30 years in our populations then divided by three, since most guidelines recommend screening for diabetes every third year.[26] The second study looked at targeted screening for gestational diabetes in antenatal settings. We used screening costs plus gestational diabetes treatment costs for positive screenings. The cost per case screened was the weighted average cost incorporating treatment costs in 9.1% of cases. (This prevalence of 9.1% in India is similar to other developing regions; a systematic review found that the prevalence in African countries ranged 1% to 13.9%.)[27]

Combination therapy for multiple risk factors and for secondary prevention after a CVRD event or diagnosis; Medical management with aspirin, beta blockers, ACE inhibitors, and statins. We conceptualized these interventions together as, 1) primary CVD prevention using a multidrug regimen among high-risk patients; 2) medical management of CVD among those without a history of acute myocardial infarction, peripheral vascular disease, or stroke; and 3) secondary CVD prevention among those with a history of acute myocardial infarction, occlusive peripheral vascular disease, or stroke. We assumed #2-3 would have a very similar cost given the overlap in medications used. Hence we took two costs from the literature: primary prevention costs and secondary prevention costs, both involving multidrug regimens as described in a multi-country CEA.[28] Based on a recent prospective multi-country study of CVD risk, we assumed that 5% of the population aged 35-74 would be classified as high-risk (>20% ten-year risk of CVD) and eligible for primary prevention.[29] From this number, we subtracted the number of prevalent cases of ischemic heart disease, stroke, and peripheral vascular disease, since these would receive secondary prevention instead. We then multiplied the first estimate by the primary prevention cost and the second estimate by the secondary prevention cost.

Use of unfractionated heparin, aspirin, and generic thrombolytics in acute events. The best studies of acute CVD treatment were two CEAs from Brazil looking at acute myocardial infarction and acute ischemic stroke.[30,31] In both cases, no invasive catheterization procedures were included in the costs we used. We multiplied these by the incidence of acute myocardial infarction and ischemic stroke.

Revascularization for acute critical limb ischemia, if available, otherwise amputation. We could not identify any economic studies of acute peripheral vascular disease in LMICs. To estimate the cost of revascularization, we used the cost of percutaneous coronary intervention as a proxy. We identified a CEA of percutaneous coronary intervention vs. medical management in Serbia and used the incremental cost of the former.[32] One important assumption we made about catheter-based procedures is that during the SDG period it will only be feasible and advisable to build interventional cardiology centers in urban areas in LMI countries. So we applied this cost to the incidence of acute peripheral vascular disease and multiplied by the proportion of the population in the LMI country living in urban areas. We did not cost revascularization for the rural LMI proportion or for the urban and rural areas of the LI country. Instead, we assumed that amputation would be the more feasible option and that (in the absence of costing studies) amputation costs for diabetic foot infections would be a reasonable proxy for vascular-related amputation. So we used amputation costs for diabetic foot in Bangladesh.[33] We calculated the cost of amputation in this study as the weighted average cost of major and minor amputations. Again, these were multiplied by the incidence of acute peripheral vascular disease in the LI country and by the incidence of acute peripheral vascular disease times the rural proportion in the LMI country.

Availability of percutaneous coronary intervention for acute myocardial infarction. Similar to the above, we used the Serbian study of percutaneous coronary intervention costs.[32] We multiplied these costs by the incidence of acute myocardial infarction times the urban proportion in the LMI country. We assumed that catheterization would not be feasible in the other settings.

Medical management with diuretics, beta-blockers, ace-inhibitors, and mineralocorticoid antagonists. We used costs from a CA of heart failure in Brazil. This study included both chronic outpatient treatment and acute inpatient treatment.[34] We multiplied the outpatient annual costs by the prevalence of chronic heart failure.

Use of diuretics and non-invasive positive pressure ventilation in acute events. We used the aforementioned study of heart failure in Brazil.[34] We multiplied the inpatient costs per hospitalization by the incidence of acute heart failure. Of note, this study did not measure the cost of non-invasive ventilation, and these estimates were not available in other LMIC country studies, so the acute heart failure costs are probably an underestimate of total inpatient costs.

Mixed vertical-horizontal insecticide spray programs to prevent Chagas disease. We used program costs from a CEA of a mixed spray program in Argentina.[35] We divided total program costs by the population served to estimate cost per capita. Because Chagas disease is only endemic to certain parts of Latin America, we did not include this cost in our main CVRD EP cost but present it as an additional cost per capita relevant only for endemic countries.

Treatment of acute pharyngitis (children) to prevent rheumatic fever; Secondary prophylaxis with penicillin for rheumatic fever or established RHD. As is recommended by WHO, we conceptualized these interventions together. A recent CEA estimated the program cost of combined primary and secondary prevention in Cuba.[36] We took the total program cost and divided by the pediatric population (5-24) in the population served to estimate the cost per at-risk child. Of note, we multiplied this cost by a factor of five to account for differences in nominal (1:1) and worst-case "actual" (1:5) exchange rates between Cuban pesos and US dollars during the study period.

Diabetes self-management education. We did not identify any formal economic evaluations of diabetes self-management programs in LMICs from the *DCP3* systematic reviews. However, we found a case study of MoPoTsyo, a diabetes peer educator group in Cambodia that estimated financial costs of peer support for self-management.[37] We divided the peer educator's financial incentive by the average number of patients served to estimate cost per case managed and multiplied by the prevalence of diabetes.

Treatment of blood pressure, lipids, and hyperglycemia; Screening and treatment for albuminuria; Consistent foot care. We conceptualized all these interventions together as part of a comprehensive diabetes care program. We used costs from a CEA of metformin in Beijing that disaggregated the costs of these relevant aspects of disease management above.[38] These were converted into costs per case managed and multiplied by the prevalence of diabetes.

Retinopathy screening via telemedicine, followed by treatment using laser photocoagulation. We used costs from a CEA of tele-retinopathy screening in South Africa.[39] The cost per case screened was the weighted average cost incorporating both program costs and laser photocoagulation costs in the minority of cases screened positive.

If transplantation available, create deceased donor programs. We could not identify any studies of the direct cost of this intervention in HIC or LMIC. However, this is largely a function

of the health system, so we assumed its costs would be subsumed as part of the health system costs that are presented below.

Treatment of proteinuric CKD with strict BP control and use of ACEI or ARBs. We used the cost of CKD management from a CEA in several Asian countries specifically comparing an ACEI to an ARB.[40] We took the costs from Thailand as the most generalizable among the countries included. We calculated a weighted average cost per case assuming that 80% would remain on an ACEI and 20% would require ARB. We then multiplied this cost per case by 75%, which is the proportion of CKD patients in India who have proteinuria (S. Anand, 2016 – personal communication).

Development of a deceased donor registry for renal transplantation. To our knowledge, no studies have produced estimates of the cost of this intervention, even in high-income countries. A similar registry in the USA would cost about $250,000 per year in a catchment area of about 30 million population (K. Willis, United Network for Organ Sharing – personal communication, 11 August 2016). We adjusted this to a cost per capita in LMICs as described below.

Annual flu vaccination and 5-yearly pneumococcal vaccine for those with underlying lung disease. We did not identify any formal economic evaluations of vaccination for chronic lung diseases in LMICs. Since these two interventions were relatively simple, and vaccines are tradeable, we calculated the cost of vaccination as the vaccine price plus the administration cost (i.e., healthcare worker's time). We used the weighted average influenza vaccine price of $4.55 per dose (see Appendix 3 of http://www.euro.who.int/__data/assets/pdf_file/0009/284832/Review-vaccine-price-data.pdf?ua=1) and the pneumococcal vaccine price of $3.50 per dose (see GAVI subsidy price at http://www.unicef.org/supply/files/PCV.pdf). The administration cost was assumed to be 5 minutes of a skilled healthcare worker's time, which we estimated using the WHO database of average salaries for LI and LMI countries (see below). Finally, we divided the pneumococcal vaccine cost per patient by five, since this cost occurs only once every five years for each patient. These costs were both multiplied by the prevalence of chronic obstructive pulmonary disease and asthma.

Low dose inhaled beta-agonists and corticosteroids for asthma. We used costs from a CEA of an asthma control program in Brazil.[41] We took the median outpatient cost per case treated following the program's implementation, then we multiplied this by the prevalence of asthma.

Oral antibiotics for patients with exacerbations of COPD. We used costs from a CA of smoking-attributable healthcare costs in Vietnam.[42] We calculated the total number of COPD hospitalizations attributable to smoking and divided the total attributable cost of COPD (government perspective) by the number of hospitalizations. This estimate of the cost of acute COPD was then multiplied by the incidence of COPD.

Further cost adjustments

After compiling estimates of intervention costs from the literature, we adjusted these costs to 2012 US dollars and then to "average" costs in low-income and lower middle-income countries. To accomplish the latter, we used an internal WHO database of healthcare worker salaries for

different skill levels for all countries (J. Serjie, 2015 – personal communication). We pooled individual country salaries to estimate average salaries for the low-income and lower middle-income regions for skilled healthcare workers, then divided country-specific unit cost estimates by either these average salaries. The ratio of regional cost to country-specific cost was then multiplied by the unit cost. This approach relies on two assumptions: 1) the components of CVRD costs are comprised predominately of non-tradeable goods and services, and 2) gradients in salary levels across countries are proportional to gradients in total costs.

The final EP was comprised of 34 interventions and policies. Estimated unit costs of each intervention for LI and LMI countries are listed in Table 1A.3.

Table 1A.3 Unit costs of EP interventions

Intervention	*LI country*	*LMI country*
Tax tobacco products	$0.002	$0.004
Improve built environment to encourage physical activity	$0.27	$0.55
School based programs to improve nutrition and encourage physical activity	$12.55	$25.37
Regulation on advertising and labeling tobacco products	$0.0002	$0.0004
Nutritional supplementation for women of reproductive age	$0.44	$0.89
Regulations to reduce salt in manufactured food products	$0.004	$0.008
Mass media health promotion targeted towards specific unhealthy foods	$0.012	$0.024
Ban trans fat	$0.001	$0.002
Promotion of healthy fats in the diet	$0.005	$0.007
Use of CHWs for screening CVRD using non-lab based tools for overall CVD risk	$0.06	$0.13
Use of community health workers for encouraging adherence to medications	$1.31	$2.66
Tobacco cessation counseling with or without nicotine replacement therapy	$10.25	$20.71
Opportunistic screening for hypertension for all adults	$5.06	$10.23
Screening for diabetes in high-risk adults	$0.83	$1.68
Screening for diabetes in pregnant women	$8.48	$17.15
CVD primary prevention in high-risk adults	$27.44	$55.48
CVD secondary prevention and medical management	$46.11	$93.20
Use of unfractionated heparin, aspirin, and generic thrombolytics in acute CVD events	$532.56	$1,076.58
Availability of percutaneous coronary intervention for acute myocardial infarction	n.a.	$1,202.17
Revascularization for acute critical limb ischemia	n.a.	$1,202.17
Amputation for acute critical limb ischemia if revascularization unavailable	$452.32	$914.37
Medical management of chronic heart failure	$328.04	$663.14
Use of diuretics and non-invasive positive pressure ventilation in acute heart failure	$481.77	$973.91

Mixed vertical-horizontal insecticide spray programs to prevent Chagas disease	$0.76	$1.53
Integrated primary and secondary prevention of rheumatic heart disease	$3.17	$6.41
Diabetes self-management education	$4.34	$8.77
Treatment of blood pressure, lipids, and hyperglycemia in diabetics	$286.56	$579.28
Screening and treatment for albuminuria in diabetics	$14.21	$28.73
Consistent foot care in diabetics	$12.81	$25.90
Retinopathy screening via telemedicine with laser photocoagulation in diabetics	$6.97	$14.08
Treatment of proteinuric CKD with strict blood pressure control and use of ACEI or ARBs	$742.41	$1,500.81
Annual flu vaccination and 5-yearly pneumococcal vaccine for asthma and COPD	$5.26	$5.28
Low dose inhaled beta-agonists and corticosteroids for asthma	$161.45	$326.38
Oral antibiotics for patients with exacerbations of COPD	$98.11	$198.33

Abbreviations: CHW = community health worker; CVRD = cardio-metabolic and respiratory disorders; CVD = cardiovascular disease; CKD = chronic kidney disease; ACEI = angiotension-converting enzyme inhibitors; ARB = angiotensin receptor blocker; COPD = chronic obstructive pulmonary disease. Note: all costs are in 2012 US dollars and represent final cost inputs based on synthesis and adjustment of literature costs. Note: costs may be expressed as cost per capita for population-wide interventions (e.g., taxes) or as cost per case for individual-level/clinical interventions (e.g., medical management of IHD).

RESULTS

The incremental cost of the EP based on the cost of the Table 1A.2 interventions ranges from $12 to $27 per capita in a low-income country and $18 to $40 per capita in a lower middle-income country. This translates to 3.4% of current per capita gross domestic product (GDP) in a low-income country and 1.5% of current per capita GDP in a lower middle-income country. Current government expenditure on health would have to increase by 134% in a LI country or 92% in a LMI country.

Table 1A.4 Estimates of EP cost in a standard population of 100,000 individuals

Estimate	*LI country*	*LMI country*
Total IC	$1,788,000	$2,635,000
Total IC per capita, mean (range)*	$18 ($12 to $27)	$26 ($18 to $40)
Proportion of current GEH	134% (89% to 201%)	92% (61% to 138%)
Proportion of GDP per capita	3.4% (2.3% to 5.2%)	1.5% (1.0% to 2.3%)

Notes: IC = incremental cost; GEH = government expenditure on health; GDP = gross domestic produce. * Range depends on the method by which "indirect" and other health system costs are accounted. All costs are in 2012 US dollars. Abbreviations: GDP = gross domestic product. GDP estimates taken from the World Bank and deflated to 2012 US dollars. GEH estimates taken from the WHO and deflated to 2012 US dollars.

We found that total chronic disease management costs were much higher than acute treatment costs ($14 vs. $2 per capita in a LI country and $15 vs. $7 per capita in a LMI country). Chronic

diabetes and kidney disease management stand out as being relatively higher than CVD, especially for the LI country, suggesting that prevention of these conditions through dietary policy could be a high priority. Asthma management was also very expensive, suggesting that reduction in environmental risk through air pollution control could be a high priority. (Air quality interventions are discussed in Volume 7 of *DCP3*).

Public health policies were generally very affordable relative to clinical interventions (total costs of $2 and $8 per capita in the LI and LMI country, respectively). However, two interventions were especially costly: improving the built environment to encourage physical activity, and increasing physical activity and education on nutrition among school-aged children. In total, the public health policies comprised 7.7% of total costs in the LI country scenario and 22.1% of total costs in the LMI country scenario. Notably, we did not include Chagas' disease vector control in these costs since the condition is confined to a few endemic areas in Latin America; the additional incremental cost per capita of the EP in that region would be $0.76 for a LI country and $1.53 for a LMI country, respectively.

IMPLICATIONS FOR PRIORITY-SETTING

The *DCP3* Volume 5 EP is fairly affordable in a typical LMI country, requiring about 1.5% of current GDP per capita to achieve UMI levels of coverage. However, if public finance were the instrument used to achieve higher levels of coverage, government expenditure on health would have to nearly double. The EP is even is less affordable in a typical LI country, requiring about 3.4% of current GDP per capita. This higher relative cost is driven by the larger coverage gap to be addressed (despite lower prices in this country).

The fact that the entire EP is less affordable in the LI country scenario suggests that a graduated approach could be taken. Such an approach could start with interventions for endemic CVRDs such as RHD, CKD, COPD, and heart failure due to non-ischemic etiologies. It could also include low-cost, high-impact policies like tobacco taxation, bans on trans fats, and regulation of tobacco advertising and salt content in processed foods. Putting in place effective population-level prevention policies that could curb the CVRD epidemic before it arrives in LI countries might actually avert a large burden of health sector spending in the long-run and lead to more rapid "convergence" in health with middle-income countries.

REFERENCES

1. WHO. One Health Tool. 2016. http://www.who.int/choice/onehealthtool/en/ (accessed 29 July 2016).
2. Nachbar J. Comparative statics. In: Durlauf SN, Blume LE, editors. The New Palgrave Dictionary of Economics Online. 2nd ed: Palgrave Macmillan; 2008.
3. Jamison DT, Summers LH, Alleyne G, et al. Global health 2035: a world converging within a generation. *Lancet* 2013; **382**(9908): 1898-955.
4. WHO. Making fair choices on the path to universal health coverage. Final report of the WHO Consultative Group on Equity and Universal Health Coverage. Geneva: World Health Organization; 2014.

5. Stenberg K, Axelson H, Sheehan P, et al. Advancing social and economic development by investing in women's and children's health: a new Global Investment Framework. *Lancet* 2014; **383**(9925): 1333-54.
6. Schwartlander B, Stover J, Hallett T, et al. Towards an improved investment approach for an effective response to HIV/AIDS. *Lancet* 2011; **377**(9782): 2031-41.
7. Bhutta ZA, Das JK, Rizvi A, et al. Evidence-based interventions for improvement of maternal and child nutrition: what can be done and at what cost? *Lancet* 2013; **382**(9890): 452-77.
8. Seshadria SR, Jha P, Sati P, Gauvreau C, Ram U, Laxminarayan R. Karnataka's roadmap to improved health: cost eff ective solutions to address priority diseases, reduce poverty and increase economic growth. Bangalore: Azim Premji University, 2015.
9. Global Burden of Disease Study. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 2015; **386**(9995): 743-800.
10. Fowkes FG, Rudan D, Rudan I, et al. Comparison of global estimates of prevalence and risk factors for peripheral artery disease in 2000 and 2010: a systematic review and analysis. *Lancet* 2013; **382**(9901): 1329-40.
11. WHO. Global health observatory (GHO) data. 2016. http://www.who.int/gho/en/ (accessed 4 June 2016).
12. UN. UN data. 2016. http://data.un.org/Default.aspx (accessed 28 June 2016).
13. AIHW. Australia Burden of Disease Study. Annex Tables. 1999. http://www.aihw.gov.au/WorkArea/DownloadAsset.aspx?id=6442459211 (accessed 28 June 2016).
14. Khatib R, McKee M, Shannon H, et al. Availability and affordability of cardiovascular disease medicines and their effect on use in high-income, middle-income, and low-income countries: an analysis of the PURE study data. *Lancet* 2016; **387**(10013): 61-9.
15. UN. Sustainable Development Goals: 17 goals to transform our world. Goal 3: Ensure healthy lives and promote well-being for all at all ages. 2016. http://www.un.org/sustainabledevelopment/health/ (accessed Feb 16 2016).
16. Gaziano T, Suhrcke M, Brouwer E, Levin C, Nikolic I, Nugent R. Summary of costs and cost-effectiveness of interventions and policies to prevent and treat cardio-metabolic diseases. In: Prabhakaran D, Gaziano T, Mbaya J, Wu Y, Anand S, Nugent R, editors. Disease Control Priorities, Third Edition Volume 5: Cardiovascular, Respiratory and Related Disorders. Washington, D. C.: World Bank; 2016.
17. Higashi H, Truong KD, Barendregt JJ, et al. Cost effectiveness of tobacco control policies in Vietnam. *Applied Health Economics and Health Policy* 2011; **9**(3): 183-96.
18. Montes F, Sarmiento OL, Zarama R, et al. Do health benefits outweigh the costs of mass recreational programs? An economic analysis of four ciclovía programs. *Journal of Urban Health* 2011; **98**(1): 153-70.
19. Meng L, Xu H, Liu A, et al. The costs and cost-effectiveness of a school-based comprehensive intervention study on childhood obesity in China. *PLoS One* 2013; **8**(10): e77971.
20. Casey GJ, Sartori D, Horton SE, et al. Weekly iron-folic acid supplementation with regular deworming is cost-effective in preventing anaemia in women of reproductive age in Vietnam. *PLoS One* 2011; **6**(9): e23723.

21. Mason H, Shoaibi A, Ghandour 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.
22. Rubinstein A, Elorriaga N, Garay OU, et al. Eliminating artificial trans fatty acids in Argentina: estimated effects on the burden of coronary heart disease and costs. *Bulletin of the World Health Organization* 2015; **93**: 614-22.
23. Gaziano T, Abrahams-Gessel S, Surka S, et al. Cardiovascular Disease Screening By Community Health Workers Can Be Cost-Effective In Low-Resource Countries. *Health affairs* 2015; **34**(9): 1538-45.
24. Gaziano TA, Bertram M, Tollman SM, Hofman KJ. Hypertension education and adherence in South Africa: a cost-effectiveness analysis of community health workers. *BMC Public Health* 2014; **14**(1): 1-9.
25. WHO. Scaling up action against noncommunicable diseases: how much will it cost? Geneva: World Health Organization; 2011.
26. Toscano CM, Duncan BB, Mengue SS, et al. Initial impact and cost of a nationwide population screening campaign for diabetes in Brazil: A follow up study. *BMC Health Services Research* 2008; **8**: 189-.
27. Macaulay S, Dunger DB, Norris SA. Gestational diabetes mellitus in Africa: a systematic review. *PLoS One* 2014; **9**(6): e97871.
28. Gaziano TA, Opie LH, Weinstein MC. Cardiovascular disease prevention with a multidrug regimen in the developing world: a cost-effectiveness analysis. *Lancet* 2006 **368**(9536): 679-86.
29. Gaziano TA, Abrahams-Gessel S, Denman CA, et al. An assessment of community health workers' ability to screen for cardiovascular disease risk with a simple, non-invasive risk assessment instrument in Bangladesh, Guatemala, Mexico, and South Africa: an observational study. *The Lancet Global health* 2015; **3**(9): e556-63.
30. Araújo DV, Teich V, Passos RBF, Martins SCO. Análise de custo-efetividade da trombólise com alteplase no Acidente Vascular Cerebral. *Arquivos Brasileiros de Cardiologia* 2010; **95**: 12-20.
31. Araújo DV, Tura BR, Brasileiro AL, Luz Neto H, Pavão ALB, Teich V. Custo-efetividade da trombólise pré-hospitalar vs intra-hospitalar no infarto agudo do miocárdio. *Arquivos Brasileiros de Cardiologia* 2008; **90**: 100-7.
32. Iva G. Cost-effectiveness analysis of percutaneous coronary intervention versus thrombolytic therapy in patients with an ST-elevated myocardial infarction. *Serbian Journal of Experimental and Clinical Research* 2011; **12**(4): 5.
33. Ali SM, Fareed A, Humail SM, et al. The personal cost of diabetic foot disease in the developing world--a study from Pakistan. *Diabetic medicine : a journal of the British Diabetic Association* 2008; **25**(10): 1231-3.
34. Araujo DV, Tavares LR, Veríssimo R, Ferraz MB, Mesquita ET. Custo da insuficiência cardíaca no Sistema Único de Saúde. *Arquivos Brasileiros de Cardiologia* 2005; **84**: 422-7.
35. Vazquez-Prokopec GM, Spillmann C, Zaidenberg M, Kitron U, Gürtler RE. Cost-Effectiveness of Chagas Disease Vector Control Strategies in Northwestern Argentina. *PLoS Neglected Tropical Diseases* 2009; **3**(1): e363.
36. Watkins DA, Mvundura M, Nordet P, Mayosi BM. A cost-effectiveness analysis of a program to control rheumatic fever and rheumatic heart disease in Pinar del Rio, Cuba. *PLoS One* 2015; **10**(3): e0121363.

37. van Olmen J, Eggermont N, van Pelt M, et al. Patient-centred innovation to ensure access to diabetes care in Cambodia: the case of MoPoTsyo. *Journal of pharmaceutical policy and practice* 2016; **9**: 1.
38. Xie X, Vondeling H. Cost-Utility Analysis of Intensive Blood Glucose Control with Metformin versus Usual Care in Overweight Type 2 Diabetes Mellitus Patients in Beijing, P.R. China. *Value in Health* 2008; **11**: S23-S32.
39. 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.
40. Annemans L, Demarteau N, Hu S, 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 : the journal of the International Society for Pharmacoeconomics and Outcomes Research* 2008; **11**(3): 354-64.
41. Franco R, Santos AC, do Nascimento HF, et al. Cost-effectiveness analysis of a state funded programme for control of severe asthma. *BMC Public Health* 2007; **7**: 82.
42. Hoang Anh PT, Thu le T, Ross H, Quynh Anh N, Linh BN, Minh NT. Direct and indirect costs of smoking in Vietnam. *Tobacco control* 2016; **25**(1): 96-100.