Health and Economic Implications of National Treatment Coverage for Cardiovascular Disease in India
Cost-Effectiveness Analysis

Sanjay Basu, MD, PhD; Eran Bendavid, MD, MS; Neeraj Sood, PhD

Background—Whether to cover cardiovascular disease costs is an increasingly pressing question for low- and middle-income countries. We sought to identify the impact of expanding national insurance to cover primary prevention, secondary prevention, and tertiary treatment for cardiovascular disease in India.

Methods and Results—We incorporated data from coverage experiments into a validated microsimulation model of myocardial infarction and stroke in India to evaluate the cost-effectiveness of alternate coverage strategies. Coverage of primary prevention alone saved 3.6 million disability-adjusted life-years (DALY) per annum at an incremental cost-effectiveness ratio of $469 per DALY averted when compared with the status quo of no coverage. Coverage of primary and secondary prevention was dominated by a strategy of covering primary prevention and tertiary treatment, which prevented 6.6 million DALYs at an incremental cost-effectiveness ratio of $2241 per DALY averted, when compared with that of primary prevention alone. The combination of all 3 categories yielded the greatest impact at an incremental cost per DALY averted of $5588 when compared with coverage of primary prevention plus tertiary treatment. When compared with the status quo of no coverage, coverage of all 3 categories of prevention/treatment yielded an incremental cost-effectiveness ratio of $1331 per DALY averted. In sensitivity analyses, coverage of primary preventive treatments remained cost-effective even if adherence and access to therapy were low, but tertiary coverage would require avoiding unnecessary procedures to remain cost-effective.

Conclusions—Coverage of all 3 major types of cardiovascular treatment would be expected to have high impact and reasonable cost-effectiveness in India across a broad spectrum of access and adherence levels. (Circ Cardiovasc Qual Outcomes. 2015;8:541-551. DOI: 10.1161/CIRCOUTCOMES.115.001994.)

Key Words: cost-effectiveness ■ developing countries ■ health policy ■ healthcare economics and organizations ■ insurance ■ myocardial infarction ■ stroke
and blood pressure medications for hypertension) is likely be highly cost-effective in LMICs. Additional studies suggested that secondary prevention of cardiovascular events through the prescribing of aspirin, blood pressure medications, and a statin for persons with a history of previous myocardial infarction or stroke would also be cost-effective in LMICs under similar assumptions of high access and adherence. However, real-world effectiveness of providing coverage for primary and secondary preventions might be more limited than suggested by these previous assessments, as studies of observed access to therapy suggest that only a minority of adults in LMICs are receiving cardiovascular treatment even when covered by insurance programs; similarly, adherence to pharmacotherapy in long-term observational cohorts averages ≈50%. We are unaware of any assessments of the cost-effectiveness of tertiary treatment for CVD events that include coverage for hospitalizations and procedures including percutaneous coronary interventions and coronary artery bypass grafting (CABG).

A recent community-based evaluation observed significant reductions in CVD mortality among patients receiving government coverage for tertiary care in a region of India than those against control regions not receiving such coverage. Given the high costs of tertiary care, several current government programs in middle-income countries such as India are offering tertiary treatment coverage as a means to avert catastrophic expenditure for families; however, it is unclear whether this is an optimal strategy for improving population health.

We used simulation models that synthesize the best available clinical and epidemiological data to estimate the health and economic implications of alternative strategies for providing national coverage for primary preventive, secondary

WHAT IS KNOWN

• Most cardiovascular disease deaths occur in low- and middle-income countries.
• National insurance programs in these countries have historically excluded coverage of cardiovascular disease therapies because the cost-effectiveness of providing such coverage has been unclear.

WHAT THE STUDY ADDS

• This study incorporates data on observed enrollment and treatment access rates after subnational expansion of insurance programs in India into a microsimulation model to assess the cost-effectiveness of public insurance coverage of cardiovascular disease therapies.
• The study reveals that coverage of all 3 major types of treatment—primary prevention, secondary prevention, and tertiary treatment—would be expected to have high impact and reasonable cost-effectiveness in India across a broad spectrum of access and adherence levels.
• Covering only secondary prevention or only tertiary treatment was not as cost-effective as strategies that incorporated primary prevention coverage.

Analytic Overview

We used an empirically validated microsimulation model to estimate the costs and benefits of expanding government healthcare insurance coverage for primary prevention, secondary prevention, and tertiary treatment of CVD among adults in India. In the status quo scenario, current access to therapy was simulated using estimates from a nationally representative survey in India. This survey revealed 17% (95% confidence interval [CI], 16%–18%) access to primary prevention therapies for cardiovascular risk factors (ie, statins and blood pressure treatments), and 54% (95% CI, 50%–58%) access to secondary prevention therapies and tertiary treatment among persons without any government insurance coverage (Table 1). To examine the benefits of expanding government insurance coverage, we assessed the expanded use of therapies after locally implemented insurance treatment coverage programs (eg, local primary preventive, secondary preventive, or tertiary treatment access schemes), which vary across populations and provinces of India. After government insurance coverage for primary prevention, access increased to 37% (95% CI, 31%–43%) on average, whereas coverage for secondary prevention or tertiary treatment increased to 75% (95% CI, 61%–88%; estimation details are available in the Data Supplement).

In our base case analysis, we evaluated the incremental health benefits and cost-effectiveness of expansion in access to care, studying primary preventive, secondary preventive, and tertiary treatment coverage in isolation and in plausible combinations. Our model outcomes included incidence and mortality from myocardial infarctions and strokes per 1000 population. We adopted a societal perspective, discounted costs and benefits by 3% annually, and expressed benefits in disability-adjusted life-years (DALYs) averted (more details on the derivation of DALYs can be found in the Data Supplement). Incremental cost-effectiveness ratios (ICER) were calculated as the additional cost in 2014 US dollars divided by the additional health benefits in DALYs associated with 1 strategy when compared with the next-less-costly cost-effective strategy. For reference, interventions are considered cost-effective if they cost less than gross domestic product (GDP) per capita per DALY averted, and cost-effective between 1× and 3× GDP per capita, where 2014 GDP per capita for India was $1523 in 2014 US dollars.

Model

Our model simulates Indians with risk factors for ischemic heart disease and cerebrovascular disease and probabilities of experiencing myocardial infarction and stroke, receiving treatment before and after such events, and dying from such events or other causes. The model has been previously validated against independent data. The population is characterized by age, sex, and residential location (urban or rural). Individuals are assigned these demographic characteristics to match demographic estimates of population size and age distribution in India from the United Nations for the year 2015; individuals then age and experience fertility and mortality, such that population size and age distribution estimates over the course of the baseline simulation match the projections from the United Nations for the period 2015 to 2035. Mortality rates in each demographic group include deaths from myocardial infarctions or strokes based on individual risk factors and from all other causes. Risk factors include...
Table 1. Values for Cardiovascular Disease Variables in the Model for India

<table>
<thead>
<tr>
<th>Variable</th>
<th>Values</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myocardial infarction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incidence (n/1000)</td>
<td>4.7–87.7</td>
<td>World Health Organization&lt;sup&gt;18&lt;/sup&gt;</td>
</tr>
<tr>
<td>Mortality (n/1000)</td>
<td>0.0–15.8</td>
<td>World Health Organization&lt;sup&gt;15&lt;/sup&gt;</td>
</tr>
<tr>
<td>Disability weight</td>
<td>0.04–0.56 (across all types; disaggregated estimates are available in the Data Supplement)</td>
<td>Global Burden of Disease Study&lt;sup&gt;19&lt;/sup&gt;</td>
</tr>
<tr>
<td>Stroke</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incidence (n/1000)</td>
<td>0.0–10.9</td>
<td>World Health Organization&lt;sup&gt;18&lt;/sup&gt;</td>
</tr>
<tr>
<td>Mortality (n/1000)</td>
<td>0.0–0.5</td>
<td>World Health Organization&lt;sup&gt;18&lt;/sup&gt;</td>
</tr>
<tr>
<td>Disability weight</td>
<td>0.01–0.74 (across all types; disaggregated estimates are available in the Data Supplement)</td>
<td>Global Burden of Disease Study&lt;sup&gt;19&lt;/sup&gt;</td>
</tr>
<tr>
<td>Treatments</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cost of thiazide ($ per y)</td>
<td>2–3</td>
<td>International Drug Price Indicator Guide&lt;sup&gt;20&lt;/sup&gt;</td>
</tr>
<tr>
<td>Cost of ACEI, enalapril ($ per y)</td>
<td>4–5</td>
<td>International Drug Price Indicator Guide&lt;sup&gt;20&lt;/sup&gt;</td>
</tr>
<tr>
<td>Cost of calcium channel blocker, amiodipine ($ per y)</td>
<td>6–7</td>
<td>International Drug Price Indicator Guide&lt;sup&gt;20&lt;/sup&gt;</td>
</tr>
<tr>
<td>Cost of aspirin ($ per y)</td>
<td>2–3</td>
<td>International Drug Price Indicator Guide&lt;sup&gt;20&lt;/sup&gt;</td>
</tr>
<tr>
<td>Cost of statin, atorvastatin ($ per y)</td>
<td>11–12</td>
<td>International Drug Price Indicator Guide&lt;sup&gt;20&lt;/sup&gt;</td>
</tr>
<tr>
<td>Cost of β-blocker, metoprolol ($ per y)</td>
<td>7–8</td>
<td>International Drug Price Indicator Guide&lt;sup&gt;20&lt;/sup&gt;</td>
</tr>
<tr>
<td>Cost of service for primary and secondary treatment, including screening, monitoring, and patient costs ($ per y)</td>
<td>5–10</td>
<td>World Health Organization&lt;sup&gt;21&lt;/sup&gt;</td>
</tr>
<tr>
<td>Cost of tertiary care services for myocardial infarction or stroke per event ($ per event)</td>
<td>160–2080</td>
<td>Community-based trial&lt;sup&gt;15&lt;/sup&gt;</td>
</tr>
<tr>
<td>Cost of postmyocardial infarction care ($ per y)</td>
<td>54–64</td>
<td>Prior cost tabulation&lt;sup&gt;22&lt;/sup&gt;</td>
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<tr>
<td>Cost of poststroke care ($ per y)</td>
<td>408–775</td>
<td>Previous cost tabulation&lt;sup&gt;22&lt;/sup&gt;</td>
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<td>Relative risk for myocardial infarction from primary prevention with ACEI and calcium channel blocker</td>
<td>0.60–0.71</td>
<td>Meta-analyses&lt;sup&gt;22–26&lt;/sup&gt;</td>
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<tr>
<td>Relative risk for stroke from primary prevention with ACEI and calcium channel blocker</td>
<td>0.45–0.58</td>
<td>Meta-analyses&lt;sup&gt;22–26&lt;/sup&gt;</td>
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<tr>
<td>Relative risk for myocardial infarction from primary prevention with statin</td>
<td>0.55–0.74</td>
<td>Meta-analyses&lt;sup&gt;22,27,28&lt;/sup&gt;</td>
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<tr>
<td>Relative risk for stroke from primary prevention with statin</td>
<td>0.78–1.00</td>
<td>Meta-analyses&lt;sup&gt;22,27,28&lt;/sup&gt;</td>
</tr>
<tr>
<td>Relative risk for myocardial infarction from secondary treatment with aspirin</td>
<td>0.60–0.72</td>
<td>Meta-analyses&lt;sup&gt;22,29,30&lt;/sup&gt;</td>
</tr>
<tr>
<td>Relative risk for stroke from secondary treatment with aspirin</td>
<td>0.72–0.84</td>
<td>Meta-analyses&lt;sup&gt;22,29,30&lt;/sup&gt;</td>
</tr>
<tr>
<td>Relative risk for myocardial infarction from secondary treatment with β-blocker</td>
<td>0.73–0.87</td>
<td>Meta-analyses&lt;sup&gt;22–26&lt;/sup&gt;</td>
</tr>
<tr>
<td>Relative risk for stroke from secondary treatment with β-blocker</td>
<td>0.68–0.74</td>
<td>Meta-analyses&lt;sup&gt;22–26&lt;/sup&gt;</td>
</tr>
<tr>
<td>Relative risk for myocardial infarction from secondary treatment with ACEI</td>
<td>0.70–0.90</td>
<td>Meta-analyses&lt;sup&gt;22–26&lt;/sup&gt;</td>
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<tr>
<td>Relative risk for stroke from secondary treatment with ACEI</td>
<td>0.56–0.84</td>
<td>Meta-analyses&lt;sup&gt;22–26&lt;/sup&gt;</td>
</tr>
<tr>
<td>Relative risk for myocardial infarction from secondary treatment with statin</td>
<td>0.62–0.82</td>
<td>Meta-analyses&lt;sup&gt;22,27,28&lt;/sup&gt;</td>
</tr>
<tr>
<td>Relative risk for stroke from secondary treatment with statin</td>
<td>0.66–1.00</td>
<td>Meta-analyses&lt;sup&gt;22,27,28&lt;/sup&gt;</td>
</tr>
<tr>
<td>Relative risk for death with secondary treatment with aspirin</td>
<td>0.81–0.89</td>
<td>Meta-analyses&lt;sup&gt;22,29,30&lt;/sup&gt;</td>
</tr>
<tr>
<td>Relative risk for death with secondary treatment with β-blocker</td>
<td>0.68–0.85</td>
<td>Meta-analyses&lt;sup&gt;22–26&lt;/sup&gt;</td>
</tr>
<tr>
<td>Relative risk for death with secondary treatment with ACEI</td>
<td>0.75–0.95</td>
<td>Meta-analyses&lt;sup&gt;22–26&lt;/sup&gt;</td>
</tr>
<tr>
<td>Relative risk for death with secondary treatment with statin</td>
<td>0.69–0.87</td>
<td>Meta-analyses&lt;sup&gt;22,27,28&lt;/sup&gt;</td>
</tr>
<tr>
<td>Relative risk of death from myocardial infarction with tertiary treatment (acute period of 28 d, then death rate subject to secondary therapy)</td>
<td>0.17–0.28</td>
<td>Community-based trial&lt;sup&gt;15&lt;/sup&gt;</td>
</tr>
<tr>
<td>Relative risk of death from stroke with tertiary treatment (acute period of 28 d, then death rate subject to secondary therapy)</td>
<td>0.42–0.80</td>
<td>Pooled randomized trials&lt;sup&gt;31–33&lt;/sup&gt;</td>
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<tr>
<td>Access and utilization to primary prevention without coverage</td>
<td>0.16–0.18</td>
<td>World Health Organization&lt;sup&gt;17&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

(Continued)
tobacco smoking, systolic blood pressure, total cholesterol, diabetes mellitus, and a previous history of myocardial infarction or stroke. These risk factors were chosen for their predictive power, their widespread availability from epidemiological studies in India, and their common usage in Indian medical practices (as discussed in the Data Supplement). The risk factor distributions are detailed across all demographic groups along with a full description of the simulation methods in Tables I to IX in the Data Supplement.

Individuals in each year of the simulation may experience myocardial infarction or stroke, based on their individual risk factors (Figure I in the Data Supplement). We adopted an alternative approach to classical (eg, Framingham) risk calculation that has been validated among diverse populations including Indians.4 The approach uses observed incidence rates relative to risk factor prevalence (Table X in the Data Supplement), rather than an absolute risk score, to calculate the relationships between incidence and risk, allowing us to calibrate the model to any given population rather than assuming universal validity of the Framingham risk equations, which are thought to misestimate risk among South Asians.4 In each year of the simulation, individuals also experienced a probability of mortality from other causes specific to their demographic cohort, based on World Health Organization (WHO) mortality estimates by cause of death.44

The model included secular trends in all variables to account for dynamic changes in risk and disease rates (Table XI in the Data Supplement) and was validated by ensuring that model estimates of myocardial infarction and stroke DALY losses and mortality were within the margin of error from independent estimates among demographic groups (Figure II in the Data Supplement).

### Coverage Scenarios

The simulated coverage strategies included primary prevention through pharmacological therapy recommended by the WHO for LMICs (Figure 1).42 As shown in Figure 1, we specifically applied the relative risk reductions associated with antihypertensive therapy to those individuals who have access to therapy (as detailed above) and would be recommended therapy per the WHO guidelines, which recommend therapy to individuals with a blood pressure >130/80 mm Hg. Those with a calculated 10-year cardiovascular event risk of 20% or above would be recommended therapy as per the WHO guidelines. Access and utilization to primary prevention would be expected to increase from 17% (95% CI, 16%–18%) without coverage to 37% (95% CI, 31%–43%) with coverage, whereas access to secondary prevention or tertiary treatment would be expected to improve from 54% without coverage (95% CI, 50%–58%) to 75% with coverage (95% CI, 61%–88%). ACEI indicates angiotensin-converting enzyme inhibitor; CI, confidence interval; and CVD, cardiovascular disease.

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**Table 1. Continued**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Values</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Access and utilization to secondary prevention or tertiary treatment</td>
<td>0.50–0.58</td>
<td>World Health Organization17</td>
</tr>
<tr>
<td>without coverage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Access and utilization to primary prevention with coverage</td>
<td>0.31–0.43</td>
<td>World Health Organization17</td>
</tr>
<tr>
<td>Access and utilization to secondary prevention or tertiary treatment</td>
<td>0.61–0.88</td>
<td>World Health Organization17</td>
</tr>
<tr>
<td>with coverage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adherence to pharmacological therapy (primary or secondary, %)</td>
<td>20–80</td>
<td>Observational cohorts34,44</td>
</tr>
</tbody>
</table>

Covariates to incidence or mortality

- Non-CVD mortality rates (n/1000) 2.5–78.7 across all age/sex/location groups; disaggregated estimates are available in Table X in the Data Supplement.
- Systolic blood pressure, mm Hg 82–177 across all age/sex/location groups; disaggregated estimates are available in Table I in the Data Supplement.
- Total cholesterol, mmol/L 3.7–8.1 across all age/sex/location groups; disaggregated estimates are available in Table II in the Data Supplement.
- Diabetes mellitus prevalence, % 0.0–6.8 across all age/sex/location groups; disaggregated estimates are available in Table II in the Data Supplement.
- Tobacco smoking, % 1.8–32.6 across all age/sex/location groups; disaggregated estimates are available in Table IV in the Data Supplement.
- History of previous myocardial infarction, % 0.7–30.4 across all age/sex/location groups; disaggregated estimates are available in Table V in the Data Supplement.
- History of previous stroke, % 0.0–0.95 across all age/sex/location groups; disaggregated estimates are available in Table VI in the Data Supplement.

Ranges represent 95% CIs across age categories, as fully disaggregated in the Data Supplement. Rates are annual rates unless otherwise noted. The cost per case is expressed in 2014 US dollars and represents the average lifetime discounted costs of disease, including all treatments (ie, the costs of procedures, hospitalizations, and medications). As in previous assessments,22 statins were modeled as conferring diminishing relative risk of myocardial infarction from 0.89 at 1 year, 0.76 at 2 years, 0.67 at 3–5 years, and 0.64 in subsequent years, and β-blocker effects included a decreasing benefit over time with the relative risk in first 3 years of 0.77 for death and 0.73 for myocardial infarction, 0.93 at 4–6 years for either outcome, and 0.99 in subsequent years for either outcome. Based on differences in utilization of services among those without and with coverage of primary, secondary or tertiary treatments for cardiovascular disease in the World Health Organization Study on Global Aging and Adult Health,17 and controlling for age, sex, urban/rural residence and income, access to primary prevention would be expected to increase from 17% (95% CI, 16%–18%) without coverage to 37% (95% CI, 31%–43%) with coverage, whereas access to secondary prevention or tertiary treatment would be expected to improve from 54% without coverage (95% CI, 50%–58%) to 75% with coverage (95% CI, 61%–88%). ACEI indicates angiotensin-converting enzyme inhibitor; CI, confidence interval; and CVD, cardiovascular disease.
others. Similarly, the guidelines recommend statin therapy to all individuals with 10-year risk >30%, patients aged >40 years with type 2 diabetes mellitus, and individuals with total cholesterol of at least 8 mmol/L (individuals likely with familial hypercholesterolemia). Secondary prevention was modeled per the WHO, which prescribes an angiotensin-converting enzyme inhibitor, aspirin, β-blocker, and statin for individuals with a history of previous myocardial infarction or stroke. Individuals surviving first myocardial infarctions or strokes during the simulation period were switched to the secondary prevention regimen. Relative risk reductions from these measures were estimated from systematic reviews and meta-analyses including Indian subjects (Table 1). Using standard approaches, we multiplied the independent relative risks of each drug by the baseline hazard of myocardial infarction to estimate overall effect on myocardial infarction and stroke incidence and mortality. We incorporated directly observed mortality risk reduction estimates from the multidrug regimens to account for the fact that some of the mortality benefits may not be through risk factor modification. We estimated the benefits of tertiary treatment as the reduction in case fatality rate among patients with myocardial infarctions and strokes in a tertiary insurance experiment in Karnataka, India (Table 1). We also included sensitivity analyses in which case fatality rates reduced further by 10% among patients presenting to tertiary care, testing sensitivity of the model to future quality improvement. Additional sensitivity analyses simulated poor quality care under expanded coverage, to determine what rate of inappropriate primary, secondary, and tertiary care (eg, conducting inappropriate procedures such as unnecessary CABG) would cause coverage to no longer be cost-effective. Note that we did not include expanded type 2 diabetes mellitus treatment in our model because glycemic control is not thought to significantly alter the primary macrovascular outcomes in our model (myocardial infarction and stroke).

Table XII in the Data Supplement provides details on the scenarios considered, which include primary prevention, secondary prevention, and tertiary treatment coverage in isolation and combination. Access to treatment before and after coverage was assessed from the nationally representative Indian cohort in the WHO Study on Global Aging and Adult Health (n=11 230), which captured changes in utilization before and after provision of insurance coverage (Table 1). Access to and utilization of primary prevention was defined as diagnosis and treatment of hypertension, hyperlipidemia, and diabetes mellitus. Access to and utilization of secondary prevention was defined as having received pharmacological treatment after survival from myocardial infarction or stroke. Access to and utilization of tertiary treatment was defined as having been able to obtain hospital-level care for acute myocardial infarction or stroke. We included scenarios in which all individuals receiving tertiary treatment were covered for secondary prevention, and scenarios in which procedural expenditures alone were covered (Table XII in the Data Supplement). We also assessed the implications of improved access, up to a range of 80% for primary and secondary preventions and tertiary treatment. Adherence to therapy was varied from a baseline value of 50% across a range from 20% to 80% as observed in previous studies of CVD pharmacotherapy. In sensitivity analyses, we calculated the minimum threshold level of adherence that would be necessary to ensure cost-effectiveness. Given the potentially diminished long-term role of β-blockers after myocardial infarction and angiotensin-converting enzyme inhibitors among patients with normal left ventricular systolic function, we also

**Figure 1.** Ischemic heart disease treatment strategies in India. Absolute risk is calculated over a 10-y horizon using the Framingham risk score, per current World Health Organization guidelines. Note that the inclusion of statin criteria of treating people with total cholesterol >8 mmol/L is meant to capture high-risk subgroups (ie, familial hypercholesterolemia). ACEI indicates angiotensin-converting enzyme inhibitor; ASA, aspirin; BP, blood pressure; and CABG, coronary artery bypass grafting.
conducted a sensitivity analysis in which only aspirin and a statin are given to patients as secondary prevention after myocardial infarction.

Costs (in 2014 US dollars; Table 1) included the direct medical costs associated with screening, diagnosis, and treatment. Tertiary hospitalization and care costs included the frequency and type of intervention, including procedures and surgeries such as percutaneous coronary intervention and CABG. Direct nonmedical costs such as patients’ out-of-pocket expenditures, time and transportation were included for all strategies. We followed up the data sources from the WHO’s CHOICE database, which are widely used, and consistent with recent subnational surveys from India. To estimate CIs, all modeled scenarios were repeated 10,000× while sampling from the ranges of input variable values, listed in Table 1. Modeling was performed in MATLAB (version R2015a; The MathWorks, Cambridge, MA).

Cost-Effectiveness Analysis

To estimate the long-term outcomes associated with coverage of CVD treatments, we projected the health and economic consequences for all cohorts of adult men and women in the first 20 years of the program, from 2015 to 2035. The ICER in terms of incremental costs per DALY averted was used as the index of cost-effectiveness.

We first compare all singular strategies (coverage of primary prevention only, secondary prevention only, or tertiary treatment only) to the status quo of no coverage. The most cost-effective singular strategy is then used as the comparator in the evaluation of cost-effectiveness of combinations of strategies, beginning with dual combinations. The series of nondenominated strategies, with increasing levels of costs and effectiveness represent the cost-effectiveness frontier. We use the term absolute dominance to refer to a strategy that is both more costly and less effective than the comparator strategy (including the strategy of maintaining the status quo), and extended dominance to refer to a strategy that is not absolutely dominated but for which the ratio of incremental costs:incremental DALYs averted is higher than that of a combination of other strategies (potentially including the status quo strategy in the combination).

Ethics Approval

Ethics committee approval for the study was obtained from the Stanford University Institutional Review Board (reference number eP-28811).

Results

Morbidity and Mortality Impact of Coverage

At existing levels of treatment in India, myocardial infarctions generated a loss of 37.9 million DALYs and strokes generated a loss of 24.6 million DALYs each year on average over the period 2015 to 2035. The DALY losses included 835,000 deaths per year from myocardial infarctions and 489,000 deaths from strokes. These model estimates reflect a 8.1 million DALY increase from the 33.1 million DALYs lost to myocardial infarctions and 21.3 million DALYs lost to strokes in the year 2012 (the most recent year estimated by the WHO), which included the effects of 734,000 deaths from myocardial infarctions and 426,000 deaths from strokes.

Coverage of primary prevention only averted 2544 DALYs per year per million population (Table 2). Coverage of primary prevention and tertiary treatment averted 4629 DALYs per year per million population or a total of 6.6 million DALYs (95% CI, 5.7–7.5 million). Coverage of primary, secondary, and tertiary treatments averted 4699 DALYs per year per million population or a total of 6.7 million DALYs (95% CI, 5.8–7.5 million; Table 2).

Cost-Effectiveness of Coverage

Table 2 and Figure 2 present the results of the cost-effectiveness analysis. As shown in Table 2, primary prevention alone for CVD costs $1.19 per capita and averted 2544 DALYs per million population each year for an ICER of $469 per DALY averted (95% CI, $355–$620) when compared with the status quo. Secondary prevention alone and tertiary treatment alone also averted DALYS at increased cost; however, each of these strategies yielded higher ICER estimates and were, therefore, extendedly dominated by primary prevention alone, which is therefore the first point on the cost-effectiveness frontier (Figure 2). Adding coverage for either secondary prevention or tertiary treatment to primary prevention coverage yielded gains with respect to DALYs averted, at increased costs and ICERs that were close in magnitude. However, the combination of primary prevention and tertiary treatment coverage had an incremental cost of $5.86 per capita and gains in DALYs averted of 4629, yielding an ICER of $2241 (95% CI, $2440–$2425), which was most favorable strategy, becoming the second point on the cost-effectiveness frontier. The strategy that covered all 3 types of care—primary and secondary prevention and tertiary treatment—compared with primary prevention plus tertiary treatment was associated with an ICER of $5588 per DALY averted and becomes the third point on the cost-effectiveness frontier (Figure 2). When compared with the status quo of no coverage, the strategy of coverage for all 3 was associated with an ICER of $1331 per DALY averted.

Sensitivity Analysis

Impact of Increased Access to Treatment

If postcoverage access to primary therapies improved from 37% in the base case analysis after insurance coverage to 50%, cost-effectiveness of primary prevention coverage would not significantly change ($472 per DALY averted), and the ICER for the combination of all 3 categories of coverage would be reduced to $2295 per DALY averted when compared with coverage for primary prevention and secondary prevention, and $1097 per DALY averted when compared with the status quo of no coverage (Table XIII in the Data Supplement). The cost-effectiveness of secondary and tertiary coverage alone or in combination was largely unaffected.

Impact of Increased Adherence to Therapy

Cost-effectiveness improved more substantially as adherence increased from the base case of 50% to 80%. With 80% adherence, cost-effectiveness of coverage for primary prevention alone improved to $288 per DALY averted (95% CI, $213–$389), whereas the ICER for the combination of all 3 categories of coverage decreased to $1796 per DALY averted relative to coverage of primary prevention and tertiary treatment (95% CI, $1481–$2110, a $3792 per DALY savings) and
to $960 per DALY averted compared with no coverage (95% CI, $756-$1219, a $371 per DALY savings; Table XIV in the Data Supplement). We estimated that 5% adherence to primary prevention therapies would be necessary for coverage of primary prevention to remain cost-effective, and a minimum of 35% adherence to secondary prevention therapies would be necessary for secondary prevention to remain cost-effective at the cost-effectiveness threshold of 3× GDP per DALY averted.

![Figure 2](http://circoutcomes.ahajournals.org/)

**Figure 2.** Efficiency frontier of alternative coverage strategies for cardiovascular disease in India. The points reveal that all 3 major types of treatment—primary, secondary, and tertiary—for cardiovascular disease would be expected to be cost-effective in India, but strategies excluding primary preventive interventions would be less efficient (lower and to the right, meaning less effective but more costly) than strategies including primary prevention. 1′ indicates primary prevention coverage; 2′, secondary treatment coverage; and 3′, tertiary treatment coverage; all, coverage of primary, secondary, and tertiary care.
Impact of Suboptimal Care
The cost-effectiveness of primary and secondary preventions was relatively insensitive to rates of inappropriate therapy, whereas tertiary treatments were more sensitive to inappropriate therapy. Even if 90% of people with new access to primary therapy received medical visits but did not receive the indicated medications for their condition (ie, providers charging for visits but not following guidelines to provide indicated medication prescriptions, as observed throughout South Asia9), primary prevention coverage would remain below the cost-effectiveness threshold because of the profound benefits of treatment at relatively low costs to the remaining 10%; by contrast, the maximum level of suboptimal benefits for secondary prevention coverage was 52%. Tertiary treatment coverage was more sensitive to inappropriate care; if >11% of patients receiving treatment were in fact receiving inappropriate therapy (ie, unnecessary procedures), then the treatment would no longer be cost-effective given the high DALY and financial costs of tertiary care.

Impact of Mortality Reduction With Tertiary Treatment
The estimated mortality benefits of tertiary treatment in the primary data set from India were 6% lower than those observed in high-income settings.10,11 There were significant improvements in cost-effectiveness with higher quality of tertiary care. With a 10% improvement in the relative risk reduction of death conferred by tertiary care (Table 1), the cost-effectiveness of tertiary care coverage alone was improved from $2253 to $1961 per DALY averted (95% CI, $1443–$2664; Figure III in the Data Supplement); the incremental cost per DALY of coverage for all 3 treatments also improved from $5588 to $2432 per DALY averted (95% CI, $523–$4341) over the cost of primary prevention and tertiary treatment alone and to $1232 per DALY averted (95% CI, $1092–$1527) over no coverage.

Impact of More Limited Secondary Prevention
If only aspirin and a statin are given to patients as secondary prevention after myocardial infarction, secondary prevention would shift from averting 148 DALYs per year per million population to averting 94.7 DALYs per year per million (95% CI, 88.7–100.6) at a cost of $0.28 per capita (95% CI, $0.25–$0.29; rather than $0.36 per capita in the baseline simulation) for a higher ICER of $2957 per DALY averted ($2485–$3269, from $2404 in the baseline simulation) relative to the status quo of no coverage. Overall this improvement did not significantly change our baseline estimates of the relative cost-effectiveness of secondary prevention alone versus the combination of primary and secondary preventions or the overall cost-effectiveness of all 3 types of therapy combined.

Discussion
Our estimates imply that universal coverage of therapies for primary prevention, secondary prevention and tertiary cardiovascular treatments would avert 6.8 million DALYs per year at the population level at a cost of ≈$1300 per DALY averted versus the status quo of no coverage. The results show that universal coverage of all 3 categories of treatment remains cost-effective under plausible scenarios about the effectiveness of coverage in improving access to care, as well as under existing estimates of adherence to therapy. Of note, currently, several Indian government-based coverage strategies are providing only tertiary coverage alone under the premise that such coverage would avert the most catastrophic expenditures; yet our analysis finds that such coverage should be expanded to include primary and secondary prevention coverage. In addition, partial coverage alone may not be capable of averting impoverishment and distress financing. Our findings also suggested that it would be particularly important to avoid the expansion of inappropriate therapies (eg, unnecessary CABG procedures) if offering tertiary treatment coverage for the coverage to remain cost-effective.

The results also show that coverage of primary prevention should be the cornerstone of any policy for universal health-care coverage of CVD and associated risk factor control. We found that all strategies that were incrementally cost-effective above less-costly strategies involved coverage of primary prevention. Coverage of primary prevention remained cost-effective even if adherence to therapy was low and even if coverage did not result in significant improvement in access to care. Coverage of primary prevention alone would save 3.6 million DALYs per year at the population level even if adherence was only 50% and access did not improve above currently observed levels; however, this outcome is significantly lower than the population level benefit of covering all treatments. Thus, coverage of primary prevention alone is only sensible in environments where coverage of all 3 treatments is simply unaffordable. We note that a fully universal plan of coverage for all 3 categories of treatment, while cost-effective, would generate a total societal cost of $13.6 billion per year (Rs. 873 billion or 87300 crore; $2.6 billion for primary prevention, $0.8 billion for secondary prevention, and $10.2 billion for tertiary treatment), most of which might have to be borne by the government to finance national coverage, which is far larger than the current $4 billion government healthcare budget; India remains among the countries with the lowest spending as a proportion of GDP (4%), despite its growing economy.12

Our results of covering primary and secondary preventions are consistent with those reported in the literature, but further enhance our understanding of actual utilization and costs, including the role of tertiary treatment coverage. Our estimates of DALYs lost to CVD are similar to independent assessments assuming continuation of the status quo in treatment access and adherence,13 as are our estimates of DALYs potentially averted from primary preventions14 and the relative impact of secondary versus primary preventive treatment.7 Our findings are the first, however, to be based on actual observed changes in access and utilization after localized coverage expansions in India, as well as directly observed risk factor values rather than imputed estimates. In addition, our study directly estimates risk reductions from tertiary care from a controlled study in India that included both the public and the private sectors,15 providing real-world estimates of care quality. Furthermore, the bulk purchasing effect of population-wide insurance programs allows us to take into account the price-lowering effect of such insurance programs on treatment costs.
Our analysis has important limitations. Data on CVD were limited to large surveys of myocardial infarctions and strokes, to the omission of less common but nevertheless prevalent forms of CVD in India such as rheumatic heart disease. Furthermore, as risk equations are updated from the traditional Framingham equations used in current WHO guidelines to versions that may compensate for the observed bias in risk calculations among South Asians, it is possible that treatment strategies will change and improve the targeting and efficacy of primary and secondary preventions among Indians. We intentionally omitted the controversial use of aspirin as a primary preventive strategy because it is explicitly excluded from recent WHO guidelines\(^1\); whereas it is widely agreed that patients at low risk of cardiovascular events should not take aspirin for primary prevention at even a low dose, 3 trials are still available to determine whether patients at higher than average risk should take low-dose aspirin.\(^2\) If those trials prove successful despite negative results in the past, then our cost-effectiveness estimates of primary preventive therapy coverage may be viewed as conservative. Our estimates of tertiary care impact are also based on a province that is considered to have less care infrastructure than some others;\(^3\) hence our cost-effectiveness estimates of tertiary treatment coverage may also be conservative for the overall country. By contrast, our estimates of the cost-effectiveness of tertiary treatment assume that there is sufficient capacity to provide it, and the cost of capacity building will be a considerable added expense in some locations that is not factored in our analysis.

Overall, coverage of primary prevention, secondary prevention, and tertiary treatment for CVD would be expected to have the largest population impact on morbidity and mortality and be cost-effective relative to the status quo of no coverage. This critically informs ongoing efforts in India and other LMICs that are seeking to expand government-based national insurance coverage strategies, but have traditionally not included coverage for noncommunicable chronic diseases that are now leading causes of catastrophic expenditure and premature morbidity and mortality.

Acknowledgments

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Disclosures

None.

References


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Supplemental Material

1 Supplemental Methods

Our objectives of this modeling work are to estimate the cost-effectiveness of primary, secondary and tertiary government-sponsored insurance coverage strategies for cardiovascular disease treatment in India. The rationale for this study is that costs and health benefits associated with population-level, long-term cardiovascular disease treatment coverage cannot be easily assessed through existing community-based cohorts, given the lack of large population-representative cohorts in low- and middle-income countries such as India, and the very long (decadal) time course of effects that effective therapies provide. Hence, modeling can integrate economic, social and epidemiological data to identify the potential benefits and risks of different decisions, as well as quantify the degree of uncertainty around such decisions, which are currently being made with incomplete data under highly uncertain conditions. The principal outcomes from this modeling work are incremental cost-effectiveness ratios related to reduced incidence and mortality from myocardial infarctions (MI) and strokes. The modeling work accounts for complex demographic, economic, and epidemiological parameters among diverse populations within India, as detailed below.

The model used in this study is an extension and expansion of a discrete-time microsimulation that we have validated and published previously 1–3, which simulates incident and recurrent MI and stroke events (both ischemic and hemorrhagic) and associated deaths, given risk factor data at the level of the individual (Supplemental Material Figure 1). The model creates a series of individual histories for members of the population being studied, spanning the time frame from the year 2015 to the year 2035. The microsimulation approach can capture the impact of population-level interventions on individual risk factor profiles, allowing for complex relationships among multiple risk factors to be taken into account, as well as multi-level environmental and social covariates (e.g., accounting for the correlations between urban residential status and healthcare access, which affects risk factor control and case fatality rates after MI or stroke).

Here, we first provide details on the design of the model, then detail its specific equations. At a macro level, the simulation first involves generating 1 million individuals representative of the demography of India, using data on the current and projected future demography of India through the year 2035 4. Each individual is defined by age (18-100), sex, and location (urban or rural). The model explicitly accounts for projected rates of fertility, migration, and mortality. New individuals enter into the population to ensure demographic stability and provide age-standardized disease rates for the entire
country as a key outcome variable. We account for both CVD mortality as well as aggregate non-CVD mortality specific to an individual’s age, sex, and location, to take into account competing risks of other diseases, and the secular changes in these risks over time. To calculate CVD morbidity and mortality, each individual in the model is assigned a starting set of risk factors for cardiovascular disease at the beginning of the simulation, which evolve as they age, and also evolve with secular trends specific to their sex and location. These risk factors (Supplemental Material Tables 1-6) are: systolic blood pressure, total cholesterol, tobacco smoking (including bidis or informal cigarettes), diabetes status, and a prior history of myocardial infarction or stroke. In a prior independent assessment, body mass index and waist-to-hip ratio were not found to significantly improve the predictive power of the model for myocardial infarction risk beyond the above-mentioned factors, hence these factors were excluded to maintain model parsimony. Similarly, diastolic blood pressure and cholesterol sub-types (low-density or high-density lipoproteins) are not widely available from population-representative Indian epidemiological studies. The risk factor profiles are specific to age, sex, location, and year, and are generated using Monte-Carlo sampling from the data obtained from the WHO Study on Global Aging and Adult Health (SAGE), Global Health Observatory, Global Burden of Disease Study, and related datasets, as detailed in the Supplemental Material Tables 1-6 following this description.

Monte Carlo sampling from these data is guided through a correlation matrix to account for the relationships between the risk factors among demographic groups and across years (e.g., capturing the correlations between diabetes and hyperlipidemia), specified in Supplemental Material Table 7. This approach implicitly captures age-by-time-by-risk-factor interactions contributing to CVD risk. We established the face validity of the estimation approach by comparing the model’s historical (backward) projections to independent estimates, which we published previously and reproduced here in Supplemental Material Figure 2.

All risk factor input data used in the model are nationally-representative data from the WHO Study on Global Aging and Adult Health (SAGE), Global Health Observatory, and Global Burden of Disease Study, as specified in Supplemental Material Tables 1 through 6. To generate each simulated individual’s risk factor profile from this data, a random number \( r \) is sampled from a normal distribution of mean 0 and standard deviation 1. For each continuous risk factor \( i \) (e.g., systolic blood pressure), the individual’s risk factor value (i.e., their individual systolic blood pressure in mmHg) is determined by the following function form:
(1) \( x_i = e^{(r \sigma_i + \mu_i)} \)

where \( x \) is the continuous risk factor value (e.g., the systolic blood pressure) for the individual for risk factor \( i \), \( \sigma \) is the transformed standard deviation of the risk factor in the individual’s cohort that year, and \( \mu \) is the transformed mean value of the risk factor in the individual’s cohort that year. The variable \( \sigma \) is multiplied by \( r \) to transform the sampled random normal distribution (mean 0 and standard deviation 1) to the standard deviation of the risk factor, then added to \( \mu \) to shift the mean of the distribution to the risk factor’s mean value. Transformations are used to correct for the right-skewed nature of the risk factor distributions. The transformations, derived previously (1), are:

(2) \( \mu_i = \ln(\omega_i^2) - \frac{\ln(\omega_i^2 + \delta_i^2)}{2} \)

and

(3) \( \sigma_i = \ln\sqrt{\ln(\delta_i^2 + e^{2\ln(\omega_i)}) - 2\ln(\omega_i)} \)

where \( \omega \) is the mean and \( \delta \) is the standard deviation of risk factor \( i \)’s distribution for the individual’s cohort that year, where their cohort is defined by age in 10-year intervals, sex, and location. For dichotomous risk factors (e.g., smoking), an individual is assigned to have that risk factor with a probability \( r \) equal to the prevalence of the risk factor in the individual’s cohort that year, using a standard binomial probability function. To capture dependence among the risk factors (e.g., to capture the fact that individuals with type 2 diabetes are also more likely to have high cholesterol), we use a multivariate normal distribution with the covariance matrix provided in Supplemental Material Table 7.

To update the risk factor profiles between years of the simulation, we carry over pre-existing conditions (e.g., diabetes) from one year to the next and track individuals over time for consistency in risk across simulation years. For example, an individual with high blood pressure will continue to have high blood pressure rather than a blood pressure randomly resampled from the population distribution each year. We also update values for age-related and secular trends (Supplemental Material Table 8).

To achieve this, we record a variable that captured the rank of each individual’s risk in the cohort (e.g., the person with highest systolic blood pressure has rank #1 in the systolic blood pressure rank list). Then the individual with the highest risk factor value
in one year obtains the highest value sampled for that risk factor in the next year from the one-year-older risk factor distributions, and the individual with the second highest risk factor value receives the second highest sample, etc. This rank-stability technique prevents survival bias during the subsequent calculations described below, as individuals who are high risk are less likely to survive to later years.  

An individual’s risk of myocardial infarction, stroke, death from each of these conditions, or death from another cause was calculated each year as a function of the individual’s risk profile. The individual’s relative hazard \( l \), the hazard of event \( j \) (non-fatal MI, non-fatal stroke, fatal MI, fatal stroke, or death from other cause) in relation to the typical hazard in their cohort that year, is defined by:

\[
\lambda_j = e^{\beta_i x_i} \sum \beta \kappa_i
\]

where \( \beta \) is the log of the relative risk of each event contributed by each risk factor \( i \) and \( x \) is the value of the risk factor for the individual that year. The log relative risks were derived from studies in India among both urban and rural populations of men and women, as detailed in Supplemental Material Table 9.

To determine individual risk from each possible event in a particular year, the population-level cohort- and year-specific event probability \( \rho \) for each event \( j \) is multiplied by the ratio of the individual’s relative hazard \( \lambda \) and the mean relative hazard \( \psi \) in that individual’s cohort that year for that event:

\[
\kappa_j = \rho_j \frac{\lambda_j}{\psi_j}
\]

where \( \kappa \) is the event probability for event \( j \) for the individual that year. A competing risks algorithm for simulating events allows us to account for multiple risks facing the same individual, including non-CVD deaths (Supplemental Material Table 10).

This also allows all-cause death to change independently of CVD-specific death, such that secular trends in non-CVD deaths can be incorporated as specified in Supplemental Material Tables 10 and 11.

Incident non-fatal MI or stroke events cause a person in the model to be reclassified as having a history of cardiovascular or cerebrovascular disease (Supplemental Material Figure 1), such that they are now subjected to the higher probability of a recurrent
event given their prior history. The ratio of non-fatal to fatal MI or stroke is adjusted each year based on the case fatality data collected by the Global Burden of Disease Study, which accounts for the probability of healthcare access, utilization, and efficacy over time by demographic group. The individual is subject to overall event risk changes subject to primary treatments if they have no prior history of myocardial infarction or stroke and have access to primary treatment (multiplying their risk by the relative risk from pharmacological therapy shown in main text Table 1), or secondary treatments if they have a history of prior myocardial infarction or stroke and have access to secondary treatment. Individuals with access to tertiary treatment also have lower 28-day acute mortality changes associated with myocardial infarction based on the relative risk reduction listed in main text Table 1, estimated from a prior cluster-randomized trial of tertiary treatment coverage in Karnataka, India. They then revert to mortality rates subject to the secondary treatment access parameters.

As found during the Global Burden of Disease study, there are several advantages to using the above framework for event rate simulation, as opposed to the older absolute risk calculation approach (e.g., Framingham risk score). There is emerging evidence that the classical risk calculation approach underestimates CVD risk among Indians, even when recalibrating the models to account for their increased risk in the presence of diabetes and/or large waist circumference; indeed, novel risk factors and biomarkers are continuously discovered and debated, though not widely assayed to incorporate into our risk calculation. By estimating the above series of equations, we only examine the relative change in actual observed CVD incidence, given a relative change in widely-assayed risk factors, which has been found to be valid in Indians and other South Asians for estimating changes in risk. Hence, we do not need to know all the risk factors affecting a group’s overall absolute CVD incidence to predict the total incidence, since current incidence trends are observed and exogenously input into the model. Furthermore, this helps policymakers to make more informed decisions for impending policies that will be decided well before any Framingham-like cohort studies are completed in India. The decisions about which primary prevention approaches to adopt through regulations are scheduled to take place years before the first set of data from any longitudinal cohorts become available.

In accordance with World Health Organization cost-effectiveness guidelines, we have chosen to use disability-adjusted life years (DALYs) as our metric of the utility gains from the simulated therapies. The DALY estimation method takes into account expected life expectancy among simulated individuals by age and sex, and uses disability weights to reflect the disutility (loss of quality of life) incurred from cardiovascular disease events. Specifically, the disability weights used in our study are those previously estimated by the Global Burden of Disease Project, which are 0.422, 95% CI: 0.284-0.56 for days 1-2 after an MI and 0.056, 95% CI: 0.035-0.082, for days 3-28 after an MI; 0.021, 95% CI: 0.011-0.037 for mild stroke, 0.076, 95% CI: 0.050-0.110 for moderate stroke,
0.312, 95% CI: 0.211-0.433 for moderate stroke with cognitive involvement, 0.539, 95% CI: 0.363-0.705 for severe stroke, and 0.567, 95% CI: 0.394-0.738 for severe stroke with cognitive involvement) 26, where the distribution of severity among strokes was taken from a prior survey of incident events in India (14.7% mild stroke, 25.8% moderate stroke without cognitive involvement, 18.6% moderate stroke with cognitive involvement, 23.7% severe stroke without cognitive involvement, and 17.2% severe stroke with cognitive involvement) 27.

To estimate the DALYs associated with incident MI and stroke, we use the following two formulas 28, which estimate the years of life lost (YLLs) due to a fatal MI or stroke event and the years of life lived with disability (YLDs) for a nonfatal MI or stroke event:

\[
YLLs = \frac{Ce^{\alpha}}{(r+\beta)^2} \left( e^{-(r+\beta)(L+a)}[-(r + \beta)(L + a) - 1] - e^{-(r+\beta)a}[-(r + \beta)a - 1] \right)
\]

and

\[
YLDs = D \frac{Ce^{\alpha}}{(r+\beta)^2} \left( e^{-(r+\beta)(L+a)}[-(r + \beta)(L + a) - 1] - e^{-(r+\beta)a}[-(r + \beta)a - 1] \right)
\]

where \( r \) = the annual discount rate (3% in our assessment), \( C \) = a constant set by the Global Burden of Disease to enhance correspondence with DALY estimates conducted before the Global Burden assessments (equal to 0.1658) 29, \( a \) = age of the event, \( \beta \) = the age weight chosen by the Global Burden of Disease (equal to 0.04), \( L \) = expected duration of life at age \( a \), which by age and sex is given by the World Health Organization’s life expectancy estimates for India in the Global Mortality Database 30, and \( D \) is the disability weight given above based on the type of event. Stroke severity was assigned probabilistically based on the distribution described above for all incident events. Total DALYs averted in a given scenario was equal to the YLLs + YLDs averted in that scenario.
## Supplemental Tables

Supplemental Material Table 1: Population distribution of systolic blood pressure

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Male urban Mean</th>
<th>SD</th>
<th>Female urban Mean</th>
<th>SD</th>
<th>Male rural Mean</th>
<th>SD</th>
<th>Female rural Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>29</td>
<td>119.3</td>
<td>13.1</td>
<td>111.4</td>
<td>13.8</td>
<td>110.1</td>
<td>13.3</td>
<td>110.2</td>
<td>14.0</td>
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<tr>
<td>30-39</td>
<td>121.9</td>
<td>20.3</td>
<td>114.3</td>
<td>16.3</td>
<td>112.5</td>
<td>19.5</td>
<td>113.1</td>
<td>16.0</td>
</tr>
<tr>
<td>40-49</td>
<td>121.0</td>
<td>24.3</td>
<td>118.6</td>
<td>17.1</td>
<td>111.6</td>
<td>22.5</td>
<td>117.4</td>
<td>17.0</td>
</tr>
<tr>
<td>50-59</td>
<td>125.2</td>
<td>21.0</td>
<td>123.6</td>
<td>15.2</td>
<td>115.4</td>
<td>20.8</td>
<td>122.4</td>
<td>15.1</td>
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<tr>
<td>60-69</td>
<td>127.2</td>
<td>17.7</td>
<td>128.0</td>
<td>12.1</td>
<td>117.4</td>
<td>17.8</td>
<td>126.6</td>
<td>12.2</td>
</tr>
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<td>&gt;70</td>
<td>130.5</td>
<td>23.8</td>
<td>129.9</td>
<td>12.6</td>
<td>120.3</td>
<td>22.7</td>
<td>128.5</td>
<td>12.5</td>
</tr>
</tbody>
</table>

Systolic blood pressure is described in mmHg from the nationally-representative WHO SAGE study. SD: standard deviation. For all Supplemental Material Tables, estimates are given for the year 2013, and for subsequent years the secular trends listed in Supplemental Material Table 8 are applied. Source: 7,9.
Supplemental Material Table 2: Population distribution of total cholesterol

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Male urban Mean</th>
<th>Male urban SD</th>
<th>Female urban Mean</th>
<th>Female urban SD</th>
<th>Male rural Mean</th>
<th>Male rural SD</th>
<th>Female rural Mean</th>
<th>Female rural SD</th>
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</thead>
<tbody>
<tr>
<td>29</td>
<td>5.45</td>
<td>1.01</td>
<td>5.33</td>
<td>0.96</td>
<td>4.82</td>
<td>0.93</td>
<td>4.70</td>
<td>0.52</td>
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<tr>
<td>30-39</td>
<td>5.51</td>
<td>1.01</td>
<td>5.46</td>
<td>1.00</td>
<td>5.08</td>
<td>0.92</td>
<td>4.89</td>
<td>0.66</td>
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<tr>
<td>40-49</td>
<td>5.67</td>
<td>1.06</td>
<td>5.75</td>
<td>1.12</td>
<td>5.13</td>
<td>0.74</td>
<td>5.10</td>
<td>0.89</td>
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<td>50-59</td>
<td>5.80</td>
<td>1.15</td>
<td>5.94</td>
<td>1.15</td>
<td>4.80</td>
<td>0.52</td>
<td>4.96</td>
<td>0.75</td>
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<tr>
<td>60-69</td>
<td>5.81</td>
<td>1.19</td>
<td>5.97</td>
<td>1.09</td>
<td>4.68</td>
<td>0.47</td>
<td>4.81</td>
<td>0.52</td>
</tr>
<tr>
<td>&gt;70</td>
<td>5.81</td>
<td>1.19</td>
<td>5.97</td>
<td>1.09</td>
<td>4.68</td>
<td>0.47</td>
<td>4.81</td>
<td>0.52</td>
</tr>
</tbody>
</table>

Total cholesterol is described in mmol/L. SD: standard deviation. For all Supplemental Material Tables, estimates are given for the year 2013, and for subsequent years the secular trends listed in Supplemental Material Table 8 are applied. Source: 

[^10]:
Supplemental Material Table 3: Population distribution of tobacco smoking

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Male urban</th>
<th>Female urban</th>
<th>Male rural</th>
<th>Female rural</th>
</tr>
</thead>
<tbody>
<tr>
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<td>11.9%</td>
<td>0.7%</td>
<td>8.7%</td>
<td>2.2%</td>
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<tr>
<td>30-39</td>
<td>22.7%</td>
<td>0.9%</td>
<td>15.5%</td>
<td>3.1%</td>
</tr>
<tr>
<td>40-49</td>
<td>32.1%</td>
<td>1.7%</td>
<td>26.6%</td>
<td>4.1%</td>
</tr>
<tr>
<td>50-59</td>
<td>36.6%</td>
<td>2.0%</td>
<td>32.9%</td>
<td>6.8%</td>
</tr>
<tr>
<td>60-69</td>
<td>32.6%</td>
<td>2.2%</td>
<td>24.1%</td>
<td>7.3%</td>
</tr>
<tr>
<td>&gt;70</td>
<td>32.6%</td>
<td>2.2%</td>
<td>24.1%</td>
<td>7.3%</td>
</tr>
</tbody>
</table>

2013 estimates based on updates to a population-representative survey of adults in Indian districts. SD: Standard deviation. For all Supplemental Material Tables, estimates are given for the year 2013, and for subsequent years the secular trends listed in Supplemental Material Table 8 are applied.
Supplemental Material Table 4: Diabetes prevalence

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Male urban Mean</th>
<th>SD</th>
<th>Female urban Mean</th>
<th>SD</th>
<th>Male rural Mean</th>
<th>SD</th>
<th>Female rural Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;29</td>
<td>5.5%</td>
<td>1.1%</td>
<td>1.2%</td>
<td>1.1%</td>
<td>3.8%</td>
<td>0.9%</td>
<td>0.8%</td>
<td>0.9%</td>
</tr>
<tr>
<td>30-39</td>
<td>10.6%</td>
<td>1.1%</td>
<td>2.2%</td>
<td>1.1%</td>
<td>4.2%</td>
<td>0.9%</td>
<td>0.9%</td>
<td>0.9%</td>
</tr>
<tr>
<td>40-49</td>
<td>14.0%</td>
<td>1.1%</td>
<td>2.9%</td>
<td>1.1%</td>
<td>6.4%</td>
<td>0.9%</td>
<td>1.3%</td>
<td>0.9%</td>
</tr>
<tr>
<td>50-59</td>
<td>14.8%</td>
<td>1.1%</td>
<td>3.1%</td>
<td>1.1%</td>
<td>6.0%</td>
<td>0.9%</td>
<td>1.3%</td>
<td>0.9%</td>
</tr>
<tr>
<td>60-69</td>
<td>18.2%</td>
<td>1.1%</td>
<td>3.8%</td>
<td>1.1%</td>
<td>15.7%</td>
<td>0.9%</td>
<td>3.3%</td>
<td>0.9%</td>
</tr>
<tr>
<td>&gt;70</td>
<td>18.2%</td>
<td>1.1%</td>
<td>3.8%</td>
<td>1.1%</td>
<td>15.7%</td>
<td>0.9%</td>
<td>3.3%</td>
<td>0.9%</td>
</tr>
</tbody>
</table>

Diabetes prevalence from a Bayesian analysis of diabetes prevalence trends \(^{12}\). SD: standard deviation. For all Supplemental Material Tables, estimates are given for the year 2013, and for subsequent years the secular trends listed in Supplemental Material Table 8 are applied.
Supplemental Material Table 5: Coronary heart disease prevalence

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Male urban Mean</th>
<th>Female urban Mean</th>
<th>Male rural Mean</th>
<th>Female rural Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SD</td>
<td>SD</td>
<td>SD</td>
<td>SD</td>
</tr>
<tr>
<td>29</td>
<td>1.38%</td>
<td>0.82%</td>
<td>1.37%</td>
<td>0.27%</td>
</tr>
<tr>
<td>30-39</td>
<td>3.01%</td>
<td>1.85%</td>
<td>3.57%</td>
<td>1.45%</td>
</tr>
<tr>
<td>40-49</td>
<td>6.54%</td>
<td>1.49%</td>
<td>8.56%</td>
<td>1.93%</td>
</tr>
<tr>
<td>50-59</td>
<td>12.78%</td>
<td>4.91%</td>
<td>13.23%</td>
<td>2.89%</td>
</tr>
<tr>
<td>60-69</td>
<td>17.37%</td>
<td>6.67%</td>
<td>17.54%</td>
<td>3.83%</td>
</tr>
<tr>
<td>&gt;70</td>
<td>17.37%</td>
<td>6.67%</td>
<td>17.54%</td>
<td>3.83%</td>
</tr>
</tbody>
</table>

Coronary heart disease prevalence is from a prior WHO meta-analysis of Indian district surveys, updated to the year 2013 based on WHO estimates of secular trends. SD: standard deviation. For all Supplemental Material Tables, estimates are given for the year 2013, and for subsequent years the secular trends listed in Supplemental Material Table 8 are applied.
<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Male urban</th>
<th>Female urban</th>
<th>Male rural</th>
<th>Female rural</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>29</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.02%</td>
<td>0.51%</td>
</tr>
<tr>
<td>30-39</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.02%</td>
<td>0.02%</td>
</tr>
<tr>
<td>40-49</td>
<td>0.05%</td>
<td>0.32%</td>
<td>0.05%</td>
<td>0.32%</td>
</tr>
<tr>
<td>50-59</td>
<td>0.58%</td>
<td>0.42%</td>
<td>0.58%</td>
<td>0.42%</td>
</tr>
<tr>
<td>60-69</td>
<td>0.88%</td>
<td>0.18%</td>
<td>0.88%</td>
<td>0.18%</td>
</tr>
<tr>
<td>&gt;70</td>
<td>0.91%</td>
<td>0.02%</td>
<td>0.91%</td>
<td>0.02%</td>
</tr>
</tbody>
</table>

Cerebrovascular disease prevalence is from a prior WHO meta-analysis of Indian district surveys, updated to the year 2013 based on WHO estimates of secular trends. SD: standard deviation. For all Supplemental Material Tables, estimates are given for the year 2013, and for subsequent years the secular trends listed in Supplemental Material Table 8 are applied.
Supplemental Material Table 7: Correlation matrix among risk factors described in SI Supplemental Material Tables 1-6

<table>
<thead>
<tr>
<th></th>
<th>Systolic blood pressure</th>
<th>Cholesterol</th>
<th>Tobacco exposure</th>
<th>Diabetes</th>
<th>Coronary heart disease</th>
<th>Cerebrovascular disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic blood</td>
<td>1.000</td>
<td>0.174</td>
<td>-0.096</td>
<td>0.087</td>
<td>0.037</td>
<td>0.045</td>
</tr>
<tr>
<td>pressure</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cholesterol</td>
<td>0.174</td>
<td>1.000</td>
<td>-0.107</td>
<td>0.098</td>
<td>0.014</td>
<td>0.012</td>
</tr>
<tr>
<td>Tobacco exposure</td>
<td>-0.096</td>
<td>-0.107</td>
<td>1.000</td>
<td>-0.034</td>
<td>-0.003</td>
<td>-0.003</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0.087</td>
<td>0.098</td>
<td>-0.034</td>
<td>1.000</td>
<td>0.037</td>
<td>0.031</td>
</tr>
<tr>
<td>Coronary heart</td>
<td>0.037</td>
<td>0.014</td>
<td>-0.003</td>
<td>0.037</td>
<td>1.000</td>
<td>0.200</td>
</tr>
<tr>
<td>disease</td>
<td>0.045</td>
<td>0.012</td>
<td>-0.003</td>
<td>0.031</td>
<td>0.200</td>
<td>1.000</td>
</tr>
</tbody>
</table>

Correlation coefficients between risk factors in the model, as provided by the Institute for Health Metrics and Evaluation from a prior assessment of risk factors based on population surveys.\(^4\)
Supplemental Material Table 8: Secular trends in risk factor levels (% change in prevalence per year). These are relative increases in the prevalence rate (not absolute increases).

<table>
<thead>
<tr>
<th>Age</th>
<th>Gender</th>
<th>Location</th>
<th>SBP</th>
<th>Chol</th>
<th>Tob exp</th>
<th>DM</th>
<th>IHD</th>
<th>Stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;29</td>
<td>Male</td>
<td>Urban</td>
<td>0.42%</td>
<td>0.21%</td>
<td>-0.01%</td>
<td>0.17%</td>
<td>0.05%</td>
<td>0.00%</td>
</tr>
<tr>
<td>30-39</td>
<td>Male</td>
<td>Urban</td>
<td>0.58%</td>
<td>0.07%</td>
<td>-0.02%</td>
<td>0.23%</td>
<td>0.05%</td>
<td>0.00%</td>
</tr>
<tr>
<td>40-49</td>
<td>Male</td>
<td>Urban</td>
<td>0.32%</td>
<td>0.04%</td>
<td>0.00%</td>
<td>0.30%</td>
<td>0.03%</td>
<td>-0.27%</td>
</tr>
<tr>
<td>50-59</td>
<td>Male</td>
<td>Urban</td>
<td>0.29%</td>
<td>0.06%</td>
<td>0.02%</td>
<td>0.07%</td>
<td>0.04%</td>
<td>-0.01%</td>
</tr>
<tr>
<td>60-69</td>
<td>Male</td>
<td>Urban</td>
<td>0.29%</td>
<td>0.07%</td>
<td>0.11%</td>
<td>0.29%</td>
<td>0.05%</td>
<td>0.01%</td>
</tr>
<tr>
<td>&gt;70</td>
<td>Male</td>
<td>Urban</td>
<td>0.29%</td>
<td>0.07%</td>
<td>-0.50%</td>
<td>0.15%</td>
<td>0.04%</td>
<td>-0.03%</td>
</tr>
<tr>
<td>&lt;29</td>
<td>Male</td>
<td>Rural</td>
<td>0.42%</td>
<td>0.21%</td>
<td>-0.01%</td>
<td>0.17%</td>
<td>0.03%</td>
<td>0.00%</td>
</tr>
<tr>
<td>30-39</td>
<td>Male</td>
<td>Rural</td>
<td>0.58%</td>
<td>0.07%</td>
<td>-0.02%</td>
<td>0.23%</td>
<td>0.05%</td>
<td>0.00%</td>
</tr>
<tr>
<td>40-49</td>
<td>Male</td>
<td>Rural</td>
<td>0.32%</td>
<td>0.04%</td>
<td>0.00%</td>
<td>0.30%</td>
<td>0.02%</td>
<td>-0.27%</td>
</tr>
<tr>
<td>50-59</td>
<td>Male</td>
<td>Rural</td>
<td>0.29%</td>
<td>0.06%</td>
<td>0.02%</td>
<td>0.07%</td>
<td>0.02%</td>
<td>-0.01%</td>
</tr>
<tr>
<td>60-69</td>
<td>Male</td>
<td>Rural</td>
<td>0.29%</td>
<td>0.07%</td>
<td>0.11%</td>
<td>0.29%</td>
<td>0.01%</td>
<td>0.01%</td>
</tr>
<tr>
<td>&gt;70</td>
<td>Male</td>
<td>Rural</td>
<td>0.29%</td>
<td>0.07%</td>
<td>-0.50%</td>
<td>0.15%</td>
<td>0.03%</td>
<td>-0.03%</td>
</tr>
<tr>
<td>&lt;29</td>
<td>Female</td>
<td>Urban</td>
<td>0.28%</td>
<td>0.25%</td>
<td>-0.15%</td>
<td>1.00%</td>
<td>0.05%</td>
<td>-0.18%</td>
</tr>
<tr>
<td>30-39</td>
<td>Female</td>
<td>Urban</td>
<td>0.48%</td>
<td>0.18%</td>
<td>-0.19%</td>
<td>0.37%</td>
<td>0.05%</td>
<td>-0.47%</td>
</tr>
<tr>
<td>40-49</td>
<td>Female</td>
<td>Urban</td>
<td>0.25%</td>
<td>0.08%</td>
<td>-0.01%</td>
<td>0.66%</td>
<td>0.02%</td>
<td>-0.11%</td>
</tr>
<tr>
<td>50-59</td>
<td>Female</td>
<td>Urban</td>
<td>0.18%</td>
<td>0.21%</td>
<td>0.22%</td>
<td>0.09%</td>
<td>0.01%</td>
<td>0.00%</td>
</tr>
<tr>
<td>60-69</td>
<td>Female</td>
<td>Urban</td>
<td>0.20%</td>
<td>0.13%</td>
<td>0.19%</td>
<td>0.16%</td>
<td>0.05%</td>
<td>0.00%</td>
</tr>
<tr>
<td>&gt;70</td>
<td>Female</td>
<td>Urban</td>
<td>0.20%</td>
<td>0.13%</td>
<td>0.19%</td>
<td>0.07%</td>
<td>0.04%</td>
<td>0.05%</td>
</tr>
<tr>
<td>&lt;29</td>
<td>Female</td>
<td>Rural</td>
<td>0.28%</td>
<td>0.25%</td>
<td>-0.15%</td>
<td>1.00%</td>
<td>0.04%</td>
<td>-0.18%</td>
</tr>
<tr>
<td>30-39</td>
<td>Female</td>
<td>Rural</td>
<td>0.48%</td>
<td>0.18%</td>
<td>-0.19%</td>
<td>0.37%</td>
<td>0.05%</td>
<td>-0.47%</td>
</tr>
<tr>
<td>40-49</td>
<td>Female</td>
<td>Rural</td>
<td>0.25%</td>
<td>0.08%</td>
<td>-0.01%</td>
<td>0.66%</td>
<td>0.03%</td>
<td>-0.11%</td>
</tr>
<tr>
<td>50-59</td>
<td>Female</td>
<td>Rural</td>
<td>0.18%</td>
<td>0.21%</td>
<td>0.22%</td>
<td>0.09%</td>
<td>0.04%</td>
<td>0.00%</td>
</tr>
<tr>
<td>60-69</td>
<td>Female</td>
<td>Rural</td>
<td>0.20%</td>
<td>0.13%</td>
<td>0.19%</td>
<td>0.16%</td>
<td>0.04%</td>
<td>0.00%</td>
</tr>
<tr>
<td>&gt;70</td>
<td>Female</td>
<td>Rural</td>
<td>0.20%</td>
<td>0.13%</td>
<td>0.19%</td>
<td>0.07%</td>
<td>0.03%</td>
<td>0.05%</td>
</tr>
</tbody>
</table>

Numbers listed describe percentage change in prevalence rates per year in each cohort from the sources described in Supplemental Material Tables 1-7. SBP = systolic blood pressure; Chol = total cholesterol; Tob exp = tobacco exposure; DM = diabetes; CHD = coronary heart disease; Stroke = cerebrovascular disease.
Supplemental Material Table 9: Relative risk per unit increase in each risk factor

Estimates are from a prior series of meta-analyses using international data. A “unit increase” is defined as a 1mmHg increase for systolic blood pressure, a 1mmol/L increase in total cholesterol, and for the dichotomous variables (any kind of tobacco use and diabetes), a unit increase is defined as going from not exposed to exposed (e.g., becoming newly diabetic, or newly starting tobacco smoking).

(A) of coronary heart disease

<table>
<thead>
<tr>
<th>Age</th>
<th>Gender</th>
<th>Location</th>
<th>SBP</th>
<th>Chol</th>
<th>Smoking</th>
<th>DM</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;29</td>
<td>Male</td>
<td>Urban</td>
<td>1.08</td>
<td>3.65</td>
<td>2.43</td>
<td>2.03</td>
</tr>
<tr>
<td>30-39</td>
<td>Male</td>
<td>Urban</td>
<td>1.07</td>
<td>3.65</td>
<td>2.43</td>
<td>2.03</td>
</tr>
<tr>
<td>40-49</td>
<td>Male</td>
<td>Urban</td>
<td>1.06</td>
<td>2.08</td>
<td>2.43</td>
<td>2.03</td>
</tr>
<tr>
<td>50-59</td>
<td>Male</td>
<td>Urban</td>
<td>1.05</td>
<td>1.55</td>
<td>1.84</td>
<td>2.03</td>
</tr>
<tr>
<td>60-69</td>
<td>Male</td>
<td>Urban</td>
<td>1.03</td>
<td>1.42</td>
<td>1.70</td>
<td>2.03</td>
</tr>
<tr>
<td>&gt;70</td>
<td>Male</td>
<td>Urban</td>
<td>1.02</td>
<td>1.42</td>
<td>1.38</td>
<td>2.03</td>
</tr>
<tr>
<td>&lt;29</td>
<td>Male</td>
<td>Rural</td>
<td>1.08</td>
<td>3.65</td>
<td>2.43</td>
<td>2.03</td>
</tr>
<tr>
<td>30-39</td>
<td>Male</td>
<td>Rural</td>
<td>1.07</td>
<td>3.65</td>
<td>2.43</td>
<td>2.03</td>
</tr>
<tr>
<td>40-49</td>
<td>Male</td>
<td>Rural</td>
<td>1.06</td>
<td>2.08</td>
<td>2.43</td>
<td>2.03</td>
</tr>
<tr>
<td>50-59</td>
<td>Male</td>
<td>Rural</td>
<td>1.05</td>
<td>1.55</td>
<td>1.84</td>
<td>2.03</td>
</tr>
<tr>
<td>60-69</td>
<td>Male</td>
<td>Rural</td>
<td>1.03</td>
<td>1.42</td>
<td>1.70</td>
<td>2.03</td>
</tr>
<tr>
<td>&gt;70</td>
<td>Male</td>
<td>Rural</td>
<td>1.02</td>
<td>1.42</td>
<td>1.38</td>
<td>2.03</td>
</tr>
<tr>
<td>&lt;29</td>
<td>Female</td>
<td>Urban</td>
<td>1.08</td>
<td>3.65</td>
<td>2.18</td>
<td>2.54</td>
</tr>
<tr>
<td>30-39</td>
<td>Female</td>
<td>Urban</td>
<td>1.07</td>
<td>3.65</td>
<td>2.18</td>
<td>2.54</td>
</tr>
<tr>
<td>40-49</td>
<td>Female</td>
<td>Urban</td>
<td>1.06</td>
<td>2.08</td>
<td>2.18</td>
<td>2.54</td>
</tr>
<tr>
<td>50-59</td>
<td>Female</td>
<td>Urban</td>
<td>1.05</td>
<td>1.55</td>
<td>2.12</td>
<td>2.54</td>
</tr>
<tr>
<td>60-69</td>
<td>Female</td>
<td>Urban</td>
<td>1.03</td>
<td>1.42</td>
<td>1.70</td>
<td>2.54</td>
</tr>
<tr>
<td>&gt;70</td>
<td>Female</td>
<td>Urban</td>
<td>1.02</td>
<td>1.42</td>
<td>1.31</td>
<td>2.54</td>
</tr>
<tr>
<td>&lt;29</td>
<td>Female</td>
<td>Rural</td>
<td>1.08</td>
<td>3.65</td>
<td>2.18</td>
<td>2.54</td>
</tr>
<tr>
<td>30-39</td>
<td>Female</td>
<td>Rural</td>
<td>1.07</td>
<td>3.65</td>
<td>2.18</td>
<td>2.54</td>
</tr>
<tr>
<td>40-49</td>
<td>Female</td>
<td>Rural</td>
<td>1.06</td>
<td>2.08</td>
<td>2.18</td>
<td>2.54</td>
</tr>
<tr>
<td>50-59</td>
<td>Female</td>
<td>Rural</td>
<td>1.05</td>
<td>1.55</td>
<td>2.12</td>
<td>2.54</td>
</tr>
<tr>
<td>60-69</td>
<td>Female</td>
<td>Rural</td>
<td>1.03</td>
<td>1.42</td>
<td>1.70</td>
<td>2.54</td>
</tr>
<tr>
<td>&gt;70</td>
<td>Female</td>
<td>Rural</td>
<td>1.02</td>
<td>1.42</td>
<td>1.31</td>
<td>2.54</td>
</tr>
</tbody>
</table>

SBP = systolic blood pressure; Chol = total cholesterol; Smoking = tobacco smoking; DM = diabetes. For dichotomous variables (e.g., diabetes), relative risk refers to the risk increase in converting from 0 (not diabetic) to 1 (diabetic).
(B) of cerebrovascular disease

<table>
<thead>
<tr>
<th>Age</th>
<th>Gender</th>
<th>Location</th>
<th>SBP</th>
<th>Chol</th>
<th>Smoking</th>
<th>DM</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;29</td>
<td>Male</td>
<td>Urban</td>
<td>1.10</td>
<td>1.48</td>
<td>2.43</td>
<td>2.00</td>
</tr>
<tr>
<td>30-39</td>
<td>Male</td>
<td>Urban</td>
<td>1.09</td>
<td>1.35</td>
<td>2.43</td>
<td>2.00</td>
</tr>
<tr>
<td>40-49</td>
<td>Male</td>
<td>Urban</td>
<td>1.08</td>
<td>1.42</td>
<td>2.43</td>
<td>2.00</td>
</tr>
<tr>
<td>50-59</td>
<td>Male</td>
<td>Urban</td>
<td>1.07</td>
<td>1.35</td>
<td>1.84</td>
<td>2.00</td>
</tr>
<tr>
<td>60-69</td>
<td>Male</td>
<td>Urban</td>
<td>1.05</td>
<td>1.25</td>
<td>1.70</td>
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</tr>
<tr>
<td>&gt;70</td>
<td>Male</td>
<td>Urban</td>
<td>1.03</td>
<td>1.09</td>
<td>1.38</td>
<td>2.00</td>
</tr>
<tr>
<td>&lt;29</td>
<td>Male</td>
<td>Rural</td>
<td>1.10</td>
<td>1.48</td>
<td>2.43</td>
<td>2.00</td>
</tr>
<tr>
<td>30-39</td>
<td>Male</td>
<td>Rural</td>
<td>1.08</td>
<td>1.42</td>
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<td>2.00</td>
</tr>
<tr>
<td>40-49</td>
<td>Male</td>
<td>Rural</td>
<td>1.07</td>
<td>1.35</td>
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</tr>
<tr>
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<td>Rural</td>
<td>1.05</td>
<td>1.25</td>
<td>1.70</td>
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</tr>
<tr>
<td>&gt;70</td>
<td>Male</td>
<td>Rural</td>
<td>1.03</td>
<td>1.09</td>
<td>1.38</td>
<td>2.00</td>
</tr>
<tr>
<td>&lt;29</td>
<td>Female</td>
<td>Urban</td>
<td>1.10</td>
<td>1.48</td>
<td>2.18</td>
<td>2.04</td>
</tr>
<tr>
<td>30-39</td>
<td>Female</td>
<td>Urban</td>
<td>1.09</td>
<td>1.35</td>
<td>2.18</td>
<td>2.04</td>
</tr>
<tr>
<td>40-49</td>
<td>Female</td>
<td>Urban</td>
<td>1.08</td>
<td>1.42</td>
<td>2.18</td>
<td>2.04</td>
</tr>
<tr>
<td>50-59</td>
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<td>Urban</td>
<td>1.07</td>
<td>1.35</td>
<td>2.12</td>
<td>2.04</td>
</tr>
<tr>
<td>60-69</td>
<td>Female</td>
<td>Urban</td>
<td>1.05</td>
<td>1.25</td>
<td>1.70</td>
<td>2.04</td>
</tr>
<tr>
<td>&gt;70</td>
<td>Female</td>
<td>Urban</td>
<td>1.03</td>
<td>1.09</td>
<td>1.31</td>
<td>2.04</td>
</tr>
<tr>
<td>&lt;29</td>
<td>Female</td>
<td>Rural</td>
<td>1.10</td>
<td>1.48</td>
<td>2.18</td>
<td>2.04</td>
</tr>
<tr>
<td>30-39</td>
<td>Female</td>
<td>Rural</td>
<td>1.09</td>
<td>1.35</td>
<td>2.18</td>
<td>2.04</td>
</tr>
<tr>
<td>40-49</td>
<td>Female</td>
<td>Rural</td>
<td>1.08</td>
<td>1.42</td>
<td>2.18</td>
<td>2.04</td>
</tr>
<tr>
<td>50-59</td>
<td>Female</td>
<td>Rural</td>
<td>1.07</td>
<td>1.35</td>
<td>2.12</td>
<td>2.04</td>
</tr>
<tr>
<td>60-69</td>
<td>Female</td>
<td>Rural</td>
<td>1.05</td>
<td>1.25</td>
<td>1.70</td>
<td>2.04</td>
</tr>
<tr>
<td>&gt;70</td>
<td>Female</td>
<td>Rural</td>
<td>1.03</td>
<td>1.09</td>
<td>1.31</td>
<td>2.04</td>
</tr>
</tbody>
</table>

SBP = systolic blood pressure; Chol = total cholesterol; Smoking = tobacco smoking; DM = diabetes. For dichotomous variables (e.g., diabetes), relative risk refers to the risk increase in converting from 0 (not diabetic) to 1 (diabetic).
Supplemental Material Table 10: Incidence and mortality rates from coronary heart disease, cerebrovascular disease, and other causes (per 1,000 per year).

<table>
<thead>
<tr>
<th>Age</th>
<th>Gender</th>
<th>Location</th>
<th>MI inc</th>
<th>Stroke inc</th>
<th>MI mort</th>
<th>Stroke mort</th>
<th>Other mort</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;29</td>
<td>Male</td>
<td>Urban</td>
<td>6.46</td>
<td>0.00</td>
<td>0.08</td>
<td>0.00</td>
<td>2.47</td>
</tr>
<tr>
<td>30-39 Male</td>
<td>Urban</td>
<td>14.13</td>
<td>0.04</td>
<td>0.19</td>
<td>0.00</td>
<td>4.21</td>
<td></td>
</tr>
<tr>
<td>40-49 Male</td>
<td>Urban</td>
<td>19.29</td>
<td>0.21</td>
<td>0.68</td>
<td>0.00</td>
<td>7.62</td>
<td></td>
</tr>
<tr>
<td>50-59 Male</td>
<td>Urban</td>
<td>51.20</td>
<td>2.21</td>
<td>2.48</td>
<td>0.04</td>
<td>15.60</td>
<td></td>
</tr>
<tr>
<td>60-69 Male</td>
<td>Urban</td>
<td>86.26</td>
<td>4.71</td>
<td>6.79</td>
<td>0.13</td>
<td>36.23</td>
<td></td>
</tr>
<tr>
<td>&gt;70 Male</td>
<td>Urban</td>
<td>81.73</td>
<td>4.24</td>
<td>15.68</td>
<td>0.17</td>
<td>78.69</td>
<td></td>
</tr>
<tr>
<td>&lt;29 Female</td>
<td>Rural</td>
<td>4.71</td>
<td>0.00</td>
<td>0.04</td>
<td>0.00</td>
<td>2.47</td>
<td></td>
</tr>
<tr>
<td>30-39 Female</td>
<td>Rural</td>
<td>7.26</td>
<td>0.04</td>
<td>0.10</td>
<td>0.00</td>
<td>4.21</td>
<td></td>
</tr>
<tr>
<td>40-49 Female</td>
<td>Rural</td>
<td>5.22</td>
<td>0.21</td>
<td>0.35</td>
<td>0.00</td>
<td>7.62</td>
<td></td>
</tr>
<tr>
<td>50-59 Female</td>
<td>Rural</td>
<td>6.47</td>
<td>2.21</td>
<td>1.23</td>
<td>0.04</td>
<td>15.60</td>
<td></td>
</tr>
<tr>
<td>60-69 Female</td>
<td>Rural</td>
<td>6.62</td>
<td>4.71</td>
<td>3.35</td>
<td>0.13</td>
<td>36.23</td>
<td></td>
</tr>
<tr>
<td>&gt;70 Female</td>
<td>Rural</td>
<td>30.93</td>
<td>4.24</td>
<td>7.88</td>
<td>0.17</td>
<td>78.69</td>
<td></td>
</tr>
<tr>
<td>&lt;29 Female</td>
<td>Urban</td>
<td>8.29</td>
<td>0.10</td>
<td>0.07</td>
<td>0.00</td>
<td>2.10</td>
<td></td>
</tr>
<tr>
<td>30-39 Female</td>
<td>Urban</td>
<td>19.10</td>
<td>0.09</td>
<td>0.08</td>
<td>0.00</td>
<td>2.55</td>
<td></td>
</tr>
<tr>
<td>40-49 Female</td>
<td>Urban</td>
<td>14.28</td>
<td>0.69</td>
<td>0.25</td>
<td>0.01</td>
<td>4.15</td>
<td></td>
</tr>
<tr>
<td>50-59 Female</td>
<td>Urban</td>
<td>20.09</td>
<td>1.97</td>
<td>1.08</td>
<td>0.05</td>
<td>9.38</td>
<td></td>
</tr>
<tr>
<td>60-69 Female</td>
<td>Urban</td>
<td>87.69</td>
<td>3.35</td>
<td>4.11</td>
<td>0.13</td>
<td>25.10</td>
<td></td>
</tr>
<tr>
<td>&gt;70 Female</td>
<td>Urban</td>
<td>86.56</td>
<td>10.90</td>
<td>12.31</td>
<td>0.53</td>
<td>60.88</td>
<td></td>
</tr>
<tr>
<td>&lt;29 Female</td>
<td>Rural</td>
<td>4.89</td>
<td>0.10</td>
<td>0.03</td>
<td>0.00</td>
<td>2.10</td>
<td></td>
</tr>
<tr>
<td>30-39 Female</td>
<td>Rural</td>
<td>7.21</td>
<td>0.09</td>
<td>0.04</td>
<td>0.00</td>
<td>2.55</td>
<td></td>
</tr>
<tr>
<td>40-49 Female</td>
<td>Rural</td>
<td>9.53</td>
<td>0.69</td>
<td>0.14</td>
<td>0.01</td>
<td>4.15</td>
<td></td>
</tr>
<tr>
<td>50-59 Female</td>
<td>Rural</td>
<td>14.56</td>
<td>1.97</td>
<td>0.55</td>
<td>0.05</td>
<td>9.38</td>
<td></td>
</tr>
<tr>
<td>60-69 Female</td>
<td>Rural</td>
<td>29.38</td>
<td>3.35</td>
<td>2.08</td>
<td>0.13</td>
<td>25.10</td>
<td></td>
</tr>
<tr>
<td>&gt;70 Female</td>
<td>Rural</td>
<td>28.55</td>
<td>10.90</td>
<td>5.96</td>
<td>0.53</td>
<td>60.88</td>
<td></td>
</tr>
</tbody>
</table>

Incidence and mortality rates are estimated using DISMOD-2 software applied to World Health Organization data \(^{13}\). For all Supplemental Material Tables, estimates are given for the year 2013, and for subsequent years the secular trends listed in Supplemental Material Table 11 are applied.
Supplemental Material Table 11: Secular trends in event rates (percent change per year)

<table>
<thead>
<tr>
<th>Age</th>
<th>Gender</th>
<th>Location</th>
<th>Heart</th>
<th>Cerebrovascular</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;29</td>
<td>Male</td>
<td>Urban</td>
<td>2.7%</td>
<td>8.0%</td>
<td>-2.5%</td>
</tr>
<tr>
<td>30-39</td>
<td>Male</td>
<td>Urban</td>
<td>2.7%</td>
<td>8.0%</td>
<td>-2.5%</td>
</tr>
<tr>
<td>40-49</td>
<td>Male</td>
<td>Urban</td>
<td>-0.9%</td>
<td>4.3%</td>
<td>-0.3%</td>
</tr>
<tr>
<td>50-59</td>
<td>Male</td>
<td>Urban</td>
<td>-0.9%</td>
<td>4.3%</td>
<td>-0.3%</td>
</tr>
<tr>
<td>60-69</td>
<td>Male</td>
<td>Urban</td>
<td>-4.5%</td>
<td>0.6%</td>
<td>2.0%</td>
</tr>
<tr>
<td>&gt;70</td>
<td>Male</td>
<td>Urban</td>
<td>-4.5%</td>
<td>0.6%</td>
<td>2.0%</td>
</tr>
<tr>
<td>&lt;29</td>
<td>Male</td>
<td>Rural</td>
<td>2.7%</td>
<td>8.0%</td>
<td>-2.5%</td>
</tr>
<tr>
<td>30-39</td>
<td>Male</td>
<td>Rural</td>
<td>2.7%</td>
<td>8.0%</td>
<td>-2.5%</td>
</tr>
<tr>
<td>40-49</td>
<td>Male</td>
<td>Rural</td>
<td>-0.9%</td>
<td>4.3%</td>
<td>-0.3%</td>
</tr>
<tr>
<td>50-59</td>
<td>Male</td>
<td>Rural</td>
<td>-0.9%</td>
<td>4.3%</td>
<td>-0.3%</td>
</tr>
<tr>
<td>60-69</td>
<td>Male</td>
<td>Rural</td>
<td>-4.5%</td>
<td>0.6%</td>
<td>2.0%</td>
</tr>
<tr>
<td>&gt;70</td>
<td>Male</td>
<td>Rural</td>
<td>-4.5%</td>
<td>0.6%</td>
<td>2.0%</td>
</tr>
<tr>
<td>&lt;29</td>
<td>Female</td>
<td>Urban</td>
<td>-5.6%</td>
<td>6.4%</td>
<td>-1.0%</td>
</tr>
<tr>
<td>30-39</td>
<td>Female</td>
<td>Urban</td>
<td>-5.6%</td>
<td>6.4%</td>
<td>-1.0%</td>
</tr>
<tr>
<td>40-49</td>
<td>Female</td>
<td>Urban</td>
<td>-7.0%</td>
<td>12.1%</td>
<td>-3.9%</td>
</tr>
<tr>
<td>50-59</td>
<td>Female</td>
<td>Urban</td>
<td>-7.0%</td>
<td>12.1%</td>
<td>-3.9%</td>
</tr>
<tr>
<td>60-69</td>
<td>Female</td>
<td>Urban</td>
<td>-8.5%</td>
<td>0.6%</td>
<td>1.9%</td>
</tr>
<tr>
<td>&gt;70</td>
<td>Female</td>
<td>Urban</td>
<td>-8.5%</td>
<td>0.6%</td>
<td>1.9%</td>
</tr>
<tr>
<td>&lt;29</td>
<td>Female</td>
<td>Rural</td>
<td>-5.6%</td>
<td>6.4%</td>
<td>-1.0%</td>
</tr>
<tr>
<td>30-39</td>
<td>Female</td>
<td>Rural</td>
<td>-5.6%</td>
<td>6.4%</td>
<td>-1.0%</td>
</tr>
<tr>
<td>40-49</td>
<td>Female</td>
<td>Rural</td>
<td>-7.0%</td>
<td>12.1%</td>
<td>-3.9%</td>
</tr>
<tr>
<td>50-59</td>
<td>Female</td>
<td>Rural</td>
<td>-7.0%</td>
<td>12.1%</td>
<td>-3.9%</td>
</tr>
<tr>
<td>60-69</td>
<td>Female</td>
<td>Rural</td>
<td>-8.5%</td>
<td>0.6%</td>
<td>1.9%</td>
</tr>
<tr>
<td>&gt;70</td>
<td>Female</td>
<td>Rural</td>
<td>-8.5%</td>
<td>0.6%</td>
<td>1.9%</td>
</tr>
</tbody>
</table>

*Global Burden of Disease estimates.*
Supplemental Material Table 12: Further details on coverage scenarios, including total annual costs (budget outlay) and DALYs given population size estimates for India for the period 2015-2035, and crude (non-incremental) cost-effectiveness ratios.

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Details</th>
<th>Total annual DALYs averted</th>
<th>Total annual costs (US$ 2014)</th>
<th>Cost-effectiveness ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary treatment coverage only</td>
<td>Access to primary treatments increases from 17% (95% CI: 16% to 18%) without coverage to 37% (95% CI: 31% to 43%) with coverage</td>
<td>3.61E+06</td>
<td>1.69E+09</td>
<td>4.69E+02</td>
</tr>
<tr>
<td>Secondary treatment coverage only</td>
<td>Access to secondary treatments increases from 54% (95% CI: 50-58%) without coverage to 75% (95% CI: 61-88%) with coverage</td>
<td>2.10E+05</td>
<td>5.04E+08</td>
<td>2.40E+03</td>
</tr>
<tr>
<td>Tertiary treatment coverage only</td>
<td>Access to tertiary treatments increases from 54% (95% CI: 50-58%) without coverage to 75% (95% CI: 61-88%) with coverage</td>
<td>2.95E+06</td>
<td>6.64E+09</td>
<td>2.25E+03</td>
</tr>
<tr>
<td>Primary and secondary coverage</td>
<td>Access to primary treatments increases from 17% (95% CI: 16% to 18%) without coverage to 37% (95% CI: 31% to 43%) with coverage, and access to secondary treatments increases from 54% (95% CI: 50-58%) without coverage to 75% (95% CI: 61-88%) with coverage</td>
<td>3.82E+06</td>
<td>2.19E+09</td>
<td>5.75E+02</td>
</tr>
<tr>
<td>Primary and tertiary coverage</td>
<td>Access to primary treatments increases from 17% (95% CI: 16% to 18%) without coverage to 37% (95% CI: 31% to 43%) with coverage, and access to secondary and tertiary treatments increases from 54% (95% CI: 50-58%) without coverage to 75% (95% CI: 61-88%) with coverage</td>
<td>6.57E+06</td>
<td>8.32E+09</td>
<td>1.27E+03</td>
</tr>
<tr>
<td>Secondary and tertiary coverage</td>
<td>Access to secondary and tertiary treatments increases from 54% (95% CI: 50-58%) without coverage to 75% (95% CI: 61-88%) with coverage</td>
<td>3.10E+06</td>
<td>7.16E+09</td>
<td>2.31E+03</td>
</tr>
<tr>
<td>All three forms of coverage</td>
<td>Access to primary treatments increases from 17% (95% CI: 16% to 18%) without coverage to 37% (95% CI: 31% to 43%) with coverage, and access to secondary and tertiary treatments increases from 54% (95% CI: 50-58%) without coverage to 75% (95% CI: 61-88%) with coverage</td>
<td>6.67E+06</td>
<td>8.87E+09</td>
<td>1.33E+03</td>
</tr>
</tbody>
</table>
Supplemental Material Table 13: Cost-effectiveness estimates if access to primary treatments improves from 37% (as in the base case) to 50%. The analysis assumes 50% adherence to pharmacological treatments, as in the base case scenario.

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Comparison to status quo</th>
<th>Incremental Analysis</th>
<th>Rational decision</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Annual DALYs averted</td>
<td>Annual cost ($US</td>
<td>R.C.E in $/DALY</td>
</tr>
<tr>
<td></td>
<td>(per million pop)</td>
<td>per capita)</td>
<td>averted relative</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>to reference</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>category</td>
</tr>
<tr>
<td>Status Quo</td>
<td>0</td>
<td>0</td>
<td>$1.96 ($1.63 to 2.29)</td>
</tr>
<tr>
<td>Primary prevention only</td>
<td>4147.77 (3443.47 to 4852.07)</td>
<td>$1.96 ($1.63 to 2.29)</td>
<td>$172 (335 to 665): INR3030 0</td>
</tr>
<tr>
<td>Secondary prevention only</td>
<td>137.56 (130.15 to 144.97)</td>
<td>$0.36 ($0.34 to $0.38)</td>
<td>$2587 (2223 to 2882): INR1661 00</td>
</tr>
<tr>
<td>Tertiary treatment only</td>
<td>2008.18 (1698.48 to 2317.88)</td>
<td>$4.68 ($3.96 to $5.4)</td>
<td>$2351 (1708 to 3180): INR1496 00</td>
</tr>
<tr>
<td>Primary + secondary</td>
<td>4328.3 (3696.8 to 4959.75)</td>
<td>$2.32 ($1.98 to $2.66)</td>
<td>$2003 (1404 to 3414): INR1286 00</td>
</tr>
<tr>
<td>Primary + tertiary</td>
<td>6241.14 (5404.03 to 6978.25)</td>
<td>$6.65 ($5.94 to $7.36)</td>
<td>$2241 (2057 to 2420): INR1439 00</td>
</tr>
<tr>
<td>Secondary + tertiary</td>
<td>2525.41 (1849.01 to 2453.87)</td>
<td>$9.06 ($8.48 to $9.24)</td>
<td>$1504 (-1706 to 1453): INR99800</td>
</tr>
<tr>
<td>All 3</td>
<td>6403.34 (5714.07 to 7092.61)</td>
<td>$7.02 ($6.26 to $7.79)</td>
<td>$2295 (1913 to 2678): INR1474 00</td>
</tr>
</tbody>
</table>

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Supplemental Material Table 14: Cost-effectiveness estimates if adherence to primary and secondary therapies improves from 50% (in the base case) to 80%. The analysis assumes 37% access to primary treatments and 75% access to secondary and tertiary care after coverage is provided, based on data from the World Health Organization Study on Global Ageing and Adult Health as in the base case.

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Comparison to status quo</th>
<th>Incremental Analysis</th>
<th>Rational decision</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Annual DALYs averted (per million pop)</td>
<td>Annual cost ($US per capita)</td>
<td>Incremental DALYs averted (per million pop)</td>
</tr>
<tr>
<td>Status Quo</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Primary prevention only</td>
<td>4109.45 (3497.17 to 4721.72)</td>
<td>$1.18 ($1.01 to $1.36)</td>
<td>4109.45 (3497.17 to 4721.72)</td>
</tr>
<tr>
<td>Secondary prevention only</td>
<td>219.78 (204.53 to 235.04)</td>
<td>$0.36 ($0.33 to $0.38)</td>
<td>219.78 (204.53 to 235.04)</td>
</tr>
<tr>
<td>Tertiary treatment only</td>
<td>2161.52 (1798.85 to 2524.19)</td>
<td>$4.55 ($3.79 to $5.31)</td>
<td>2161.52 (1798.85 to 2524.19)</td>
</tr>
<tr>
<td>Primary + secondary</td>
<td>4294.46 (3730.87 to 4858.04)</td>
<td>$1.55 ($1.35 to $1.75)</td>
<td>185.01 (130.32 to 233.7)</td>
</tr>
<tr>
<td>Primary + tertiary</td>
<td>6126.75 (5297.41 to 6956.1)</td>
<td>$5.72 ($4.94 to $6.49)</td>
<td>1832.3 (1566.54 to 2098.05)</td>
</tr>
<tr>
<td>Secondary + tertiary</td>
<td>2279.27 (2180.81 to 2377.72)</td>
<td>$4.91 ($4.7 to $5.12)</td>
<td>-1830.18 (-2344 to -1316.36)</td>
</tr>
<tr>
<td>All 3</td>
<td>6326.22 (5586.64 to 7065.8)</td>
<td>$6.68 ($5.37 to $8.79)</td>
<td>199.46 (109.7 to 289.22)</td>
</tr>
</tbody>
</table>

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3 Supplemental Figures and Figure Legends

Supplemental Material Figure 1: Model flow diagram
Supplemental Material Figure 2: Face validity of model versus WHO estimates.
Supplemental Material Figure 3: Efficiency frontier of alternative coverage strategies for cardiovascular disease in India following a 10% improvement in tertiary care outcomes, conferring a relative risk reduction for mortality following myocardial infarction of 74% as compared to the base case of 64%, and a relative risk reduction for mortality following stroke of 50% as compared to a base case of 40%.

1' = primary treatment coverage, 2' = secondary treatment coverage, 3' = tertiary treatment coverage, all = coverage of primary, secondary, and tertiary care.
Supplemental References


23. Teo K, Chow CK, Vaz M, Rangarajan S, Yusuf S. The Prospective Urban Rural Epidemiology (PURE) study: Examining the impact of societal influences on chronic


