Diabetes, cardiovascular disease, and chronic kidney disease in South Asia: current status and future directions

South Asians are more susceptible to diabetes and cardiovascular diseases and have worse outcomes than other ethnicities, say Anoop Misra, Tazeen Jafar, and colleagues. They call for urgent action to provide screening and treatment, complemented by population level lifestyle modifications.

**Methods**
We gathered data on characteristics of populations and health systems from publicly available World Bank reports and WHO’s country profiles. Information on death and disability from cardiovascular disease, diabetes, and chronic kidney disease and their attributable risk factors came from Health Metrics and Evaluation’s data visualisation tool of the Global Burden of Disease Study 2015. We searched PubMed and Google Scholar for relevant literature up to January 2017, using the terms “South Asians”, “diabetes”, “cardiovascular disease”, “myocardial infarction”, “stroke”, “renal”, and “kidney disease”. We formulated this paper by drawing from our collective experience in this field and the available literature.

**Current epidemiology and trends**
Cardiovascular disease, diabetes, and chronic kidney disease now account for 27%, 4.0%, and 3.0% of deaths, respectively, in South Asia (table 1).14 Notwithstanding the limited quality and breadth of data, ischaemic heart disease is the leading cause of death in India, Pakistan, Nepal, and Sri Lanka, and stroke is the leading cause in Bangladesh.

The age standardised years of life lost as a result of cardiovascular disease has increased in South Asia in contrast to most other regions, where the reverse is true.7 In part, this is because cardiovascular disease events are more common in South Asia than in high income countries.7,8 Furthermore, acute myocardial infarction occurs six years earlier in South Asians than in European counterparts, probably owing to earlier onset of risk factors. Case fatality rates are higher in South Asia, especially in younger adults, thereby increasing the years of life lost.7,8 Stroke and chronic kidney disease may also occur earlier in South Asians.9,10 The effect of lives lost due to premature cardiovascular disease is far worse in South Asia than elsewhere, as more than half of the population lives in conditions of poverty.1

**Susceptibility to diabetes, cardiovascular diseases, and chronic kidney disease**
The region has experienced rapid demographic, epidemiological, environmental, and economic transitions. These, coupled with unhealthy lifestyles of physical inactivity and consumption of a calorie dense diet, have increased the risk of non-communicable diseases. In addition, social disparities, wealth inequalities, and conflicts in the region contribute to high rates of stress associated behaviours including smoking.31,32 Evidence from multi-country case-control studies indicates that hypertension, dyslipidaemia, smoking, obesity, diabetes, physical inactivity, low fruit and vegetable intake, and psychosocial stress attribute up to 90% of the population risk of cardiovascular disease in South Asians.13,14 Age standardised blood pressure and cholesterol levels and prevalence of diabetes have increased in South Asia over the past decades.15,16 High blood pressure and high blood glucose are the leading attributable risk factors for deaths from chronic kidney disease in every South Asian country (table 2).

Adverse metabolic factors are evident in South Asians at an early age. South Asian children have been shown to have adverse metabolic factors (hyperinsulinaemia, dyslipidaemia) compared with British children of similar age and body mass index and higher blood pressure than white children in the US,18,19 Physical inactivity, dietary imbalances, and increasing obesity amplify this (fig 1).10,21

South Asian adults have greater risks of cardiovascular disease and diabetes, both of which tend to manifest around 5-10 years earlier than in white Europeans.10 The risk of cardiovascular disease is independent of that predicted by established risk factors. Possible mechanisms, among others, include an atherogenic dyslipidaemia driven by high concentrations of triglycerides and low concentrations of high density lipoprotein cholesterol, a pro-coagulant tendency, and higher concentrations of inflammatory cytokines.22 Further work is needed to define mechanisms for this excess cardiovascular disease risk. The risk factors vary by socioeconomic strata, geographical region, and migration.

Of particular importance, South Asian adults are more insulin resistant at any given body mass index and may experience more
HEALTH IN SOUTH ASIA

Table 1 | Population characteristics and burden of cardiovascular diseases and diabetes in South Asia

<table>
<thead>
<tr>
<th>Population characteristics</th>
<th>Bangladesh</th>
<th>India</th>
<th>Nepal</th>
<th>Pakistan</th>
<th>Sri Lanka</th>
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</thead>
<tbody>
<tr>
<td>Population (millions)</td>
<td>161.9</td>
<td>131.0</td>
<td>28.5</td>
<td>189.0</td>
<td>21.0</td>
</tr>
<tr>
<td>Rural population, %</td>
<td>65.7</td>
<td>67.3</td>
<td>81.4</td>
<td>61.2</td>
<td>81.6</td>
</tr>
<tr>
<td>Life expectancy at birth, years</td>
<td>71.6</td>
<td>68.0</td>
<td>69.6</td>
<td>66.2</td>
<td>74.8</td>
</tr>
<tr>
<td>Population living on &lt;$3/day PPP, %</td>
<td>NA</td>
<td>58.1</td>
<td>48.3</td>
<td>45.0</td>
<td>14.0</td>
</tr>
<tr>
<td>Overweight/obese (BMI ≥25, 20 years), age standardised %</td>
<td>18.1</td>
<td>22.0</td>
<td>18.0</td>
<td>23.0</td>
<td>25.2</td>
</tr>
<tr>
<td>Hypertension (218 years), age standardised %</td>
<td>25.7</td>
<td>25.4</td>
<td>26.4</td>
<td>26.6</td>
<td>21.2</td>
</tr>
<tr>
<td>Diabetes, age standardised %</td>
<td>9.2</td>
<td>8.3</td>
<td>9.5</td>
<td>12.1</td>
<td>7.6</td>
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Age standardised CVD and diabetes death rates 1

<table>
<thead>
<tr>
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<th>Pakistan</th>
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</thead>
<tbody>
<tr>
<td>CVD death rate per 100,000</td>
<td>363.9</td>
<td>352.6</td>
<td>295.2</td>
<td>530.9</td>
<td>239.9</td>
</tr>
<tr>
<td>CVD death rate, % of total deaths</td>
<td>36.5</td>
<td>30.4</td>
<td>29.6</td>
<td>44.0</td>
<td>38.0</td>
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<tr>
<td>Ischemic heart disease, % of all deaths in 2015</td>
<td>15.9</td>
<td>17.6</td>
<td>17.4</td>
<td>28.4</td>
<td>20.8</td>
</tr>
<tr>
<td>Stroke, % of all deaths in 2015</td>
<td>18.3</td>
<td>8.9</td>
<td>8.8</td>
<td>11.6</td>
<td>12.8</td>
</tr>
<tr>
<td>Diabetes death rate per 100,000 in 2015</td>
<td>67.1</td>
<td>43.3</td>
<td>35.7</td>
<td>53.0</td>
<td>50.9</td>
</tr>
<tr>
<td>Diabetes death rate, % of total deaths</td>
<td>6.7</td>
<td>3.7</td>
<td>3.6</td>
<td>4.4</td>
<td>8.1</td>
</tr>
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Table 2 | Age standardised deaths from chronic kidney disease (CKD) and major attributable risk factors in South Asia 3

<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td>Age standardised CKD death rate 1</td>
<td>21.78</td>
<td>38.87</td>
<td>18.66</td>
<td>24.27</td>
<td>22.54</td>
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<tr>
<td>Rate per 100,000</td>
<td>2.2</td>
<td>3.4</td>
<td>1.6</td>
<td>2.4</td>
<td>3.6</td>
</tr>
<tr>
<td>% of total deaths</td>
<td>2.2</td>
<td>3.4</td>
<td>1.6</td>
<td>2.4</td>
<td>3.6</td>
</tr>
</tbody>
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Risk factor attributions for CKD

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</tr>
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<tr>
<td>Systolic blood pressure, %</td>
<td>67.4</td>
<td>69.4</td>
<td>70.5</td>
<td>73.9</td>
<td>83.1</td>
</tr>
<tr>
<td>Fasting blood glucose, %</td>
<td>54.4</td>
<td>59.4</td>
<td>56.1</td>
<td>54.5</td>
<td>47.8</td>
</tr>
<tr>
<td>High body mass index, %</td>
<td>11.0</td>
<td>14.5</td>
<td>23.7</td>
<td>16.6</td>
<td>18.6</td>
</tr>
</tbody>
</table>

Fig 1 | Interacting risk pathways contributing to higher risks of diabetes and cardiovascular disease (CVD) in South Asians, acting over the life course. This begins with poor maternal nutrition and adverse programming, with neonates born at lower average birth weights yet higher fat to lean mass ratios compared with white children. This phenotype worsens over time, with greater weight gain and lower activity levels in South Asian children and adults, leading, in turn, via greater insulin resistance and CVD risk factors, to higher rates of diabetes and CVD, respectively. The parallel societal, political, and health considerations, as well as life course considerations, are also shown. BMI=body mass index; BP=blood pressure; CVD=chronic kidney disease.

Health policies are not geared to respond to the rising challenge

Non-communicable diseases have been a recent addition to the policy agenda in all South Asian countries. Public health expenditures vary across countries, but overall investment is insufficient to support services for the prevention and management of cardiovascular disease, diabetes, and chronic kidney disease (table 3). Implementation has been slow owing to donor agencies having limited interest in investing in non-communicable diseases and lack of engagement between governments and professional organisations in this field.

is, at lower levels of glycaemia. This requires wider testing and earlier use of antihyperglycaemic treatment, complemented with population-wide strategies to drive change in dietary habits and physical activity. Although antihypertensive, antidiabetic, and lipid lowering drugs are part of WHO’s list of essential medicines, availability in government primary care facilities is poor and patients must often pay out of pocket for these drugs. Social insurance schemes in countries are not available to the majority of the population, and they tend to cover hospital based treatment and do not provide for standardised screening and medical management of these conditions in primary care.

Under-diagnosis and under-treatment result in higher rates of myocardial infarction and stroke, with adverse outcomes due to poor access to standardised and affordable treatment. Most patients with acute ischaemic heart disease are brought to the hospital too late to qualify for reperfusion therapy. Management in primary care is less than satisfactory, and many patients do not receive appropriate drugs owing to gaps in the knowledge and practices of healthcare providers. The situation is much worse in rural areas, where an acute event is more likely to be fatal.

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In India, the National Programme for Prevention and Control of Cancer, Diabetes, CVD and Stroke has piloted opportunistic screening of risk factors for non-communicable diseases for people over 30 years of age. Furthermore, as part of the national health mission, the Indian government has outlined an operational plan for universal screening for hypertension and diabetes. A model of opportunistic screening for diabetes in patients with tuberculosis is being evaluated in Sri Lanka. Examples of successful public-private partnerships for non-communicable disease healthcare in the region are limited. Pakistan’s National Action Plan for Non-communicable Diseases is one such model, which involved a tripartite collaboration with Heartfile, a not for profit organisation, in formulation of policy and implementation in partnership with the government and WHO.

**Recommendations**

Progress towards the targeted reductions in death and disability from cardiovascular disease, diabetes, and chronic kidney disease would not be possible without concerted, multi-sectoral efforts by various government entities and non-government partners. We recommend the following essential policy and health system interventions.

**Implementation of taxes on unhealthy foods**

A tax of 20% on sugar sweetened drinks in India is projected to reduce the prevalence of overweight and obesity by 3.0% (95% confidence interval 1.6% to 5.9%) and the incidence of type 2 diabetes by 1.6% (1.2% to 1.9%) over the period 2014-23, assuming that consumption increases in line with current trends. In Mexico, an excise tax of 10% on sugar sweetened drinks decreased consumption by an average of 6% over one year. The Indian state of Kerala recently announced a “fat tax” on pizzas, burgers, sandwiches, and tacos sold through branded food outlets. Such strategies must be adopted in cities of South Asia that experience widespread marketing and consumption of unhealthy fast foods.

Furthermore, a 20% tax on palm oil purchases in India is projected to avert approximately 363,000 (95% confidence interval 247,000 to 479,000) deaths from myocardial infarctions and strokes over the period 2014-23 (1.3% reduction in cardiovascular deaths). Palm oil is consumed widely in low and middle income countries. It is high in saturated fat and causes a large increase in cholesterol concentrations. Empirical data from Mauritius show a reduction of 1 mmol/L in cholesterol concentrations in 2011 (none since then) from doctors to community healthcare workers holds promise and is being tested in rural areas in South Asia. Studies from Pakistan and India have shown that involving trained health workers in home health education on diet and physical activity and training general practitioners led to earlier diagnosis and better management of patients with hypertension or diabetes, and it was also cost effective.

**Strengthening of health system capacity to deliver care for non-communicable diseases**

Strengthening of health systems and a well designed quality of care improvement framework are essential for concerted efforts to manage hypertension and diabetes for prevention of cardiovascular disease and chronic kidney disease. Shifting management of chronic diseases and risk factors from doctors to community healthcare workers holds promise and is being tested in rural areas in South Asia. Studies from Pakistan and India have shown that involving trained health workers in home health education on diet and physical activity and training general practitioners led to earlier diagnosis and better management of patients with hypertension or diabetes, and it was also cost effective. Scaling up similar models is likely to offer substantial reductions in cardiovascular disease and chronic kidney disease in the medium to long term.

Screening populations at high risk (such as people who are sedentary, overweight, or smokers; those with hypertension; those with a family history of diabetes or premature cardiovascular disease in first degree relatives; and women with a history of gestational diabetes) is essential for early diagnosis. Low cost strategies such as validated simple screening questionnaires, blood pressure measurement, and, if possible, fasting or random blood glucose
measurement, urinary dipstick for protein, and non-fasting cholesterol measurement, may be used. Although the cost effectiveness of opportunistic screening compared with universal screening is likely to vary according to the characteristics of the population, its value cannot be overstated for countries with a high prevalence of diabetes.58

Making antihypertensives, statins, and diabetes drugs available for free or at low cost in primary healthcare centres should be prioritised. This is consistent with achievement of universal health coverage, including access to quality and affordable essential medicines for all, as advocated in the United Nations’ sustainable development goals.49 High quality generic drugs produced in the region can help to make this sustainable. Fixed dose drug combinations may improve coverage and long term adherence in people with established disease, but their widespread use in primary prevention is still debated.50 Health insurance reforms must provide for screening and primary care for these conditions to reduce out of pocket expenditure.51 Evidence is growing for m-health (mobile health technologies) interventions in improving adherence to treatment, maintaining appointments, data collection, and supporting health workers.52 More than 80% of the population of South Asia have mobile phones, and a large majority of villages are connected with mobile technology.53 This platform should be strongly considered in risk communication strategies and integration of care delivery for non-communicable diseases where feasible. Public-private partnerships for non-communicable disease care should be encouraged to provide for unmet needs. Setting standards for long term public sector engagement; having transparent goals, inputs, and expectations; good governance of costs and fair allocation of profits; a shared vision and trust; and agreed processes for negotiation on common interests of partners are crucial to their success. The Sindh Institute of Urology and Transplantation in Karachi, Pakistan, providing dialysis services, and Aravind Eye Care System in India are good examples of successful public-private partnerships in the region.54-55

Consideration of population based strategies to promote a healthy lifestyle Community based interventions to promote a healthy diet and physical activity and reduce smoking and stress will go a long way in delaying the onset of these diseases. The Indian Diabetes Prevention Program, and more recently the D-CLIP study, showed the effectiveness of lifestyle intervention in reducing the development of diabetes in people at high risk, while concurrently tackling problems with community acceptability and long term sustainability.56-57 School health programmes, encouraged by WHO to inform children about risk factors for non-communicable diseases and promote physical activity, have been hindered by low education budgets and poor infrastructure. There are no restrictions on advertising unhealthy food to minors.58 Such legislation must be complemented with multi-sectoral action including involvement of schools and workplaces to influence diet and physical activity.

Investment in surveillance and research Surveillance and monitoring are critical to raise awareness and inform policy and implementation. Although the WHO STEPS instrument (www.who.int/chp/steps/instrument/en/) for collecting data on risk factors for non-communicable diseases has been used in community based studies in South Asia, national implementation is lacking.59 All South Asian countries must institution-alise risk factor surveillance and establish robust cardiovascular disease, diabetes, and chronic kidney disease registries to track trends and monitor progress. Surveillance data must be shared publicly to create awareness.

Evidence on effective interventions to prevent and control non-communicable diseases in the region is very limited. The effect of school, workplace, and community based interventions must be evaluated. Research comparing single versus multiple risk factor screening, as well as opportunistic and targeted screening versus universal screening in all adults, will help to tailor screening strategies. Policy initiatives such as taxes and diet substitution must be rigorously evaluated for their feasibility and impact at a population level.

Conclusion Capacity building, financing, and a strong quality assurance framework are crucial for the effectiveness, scalability, and long term sustainability of initiatives to curb non-communicable diseases in the South Asia region. Contributors: AM and THJ drafted an outline for the concept note and the full paper. All co-authors contributed in an interactive process to the various sections of the drafts and approved the final version. Competing interests: We have read and understood BMJ policy on declaration of interests and have no relevant interests to declare.

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