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# 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.

All South Asian countries have adopted the World Health Organization's Global Action Plan for the Prevention and Control of Non-Communicable Diseases, which recommends a 25% relative reduction in the prevalence of raised blood pressure by 2025 and a halt to the rise in diabetes and obesity. Although considerable diversity exists between countries, all South Asians have markedly elevated risks of diabetes and variably elevated risks of cardiovascular disease compared with other ethnicities.<sup>12</sup> In this paper, we review the burden of diabetes, cardiovascular disease, and chronic kidney disease in the region and policies to mitigate this burden. We identify key actions for health authorities and governments to attenuate the rise in non-communicable diseases and meaningfully improve outcomes for the millions of people with, or expected to develop, these diseases.

## 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).<sup>3-6</sup> 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.<sup>5</sup> In part, this is because cardiovascular disease events are more common in South Asia than in high income countries.<sup>7,8</sup> 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.<sup>7,8</sup> Stroke and chronic kidney disease may also occur earlier in South Asians.<sup>9-11</sup> 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.<sup>3</sup>

## 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.<sup>11,12</sup> 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.<sup>13,14</sup> Age standardised blood pressure and cholesterol levels and prevalence of diabetes have increased in South Asia over the past decades.<sup>15-17</sup> 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.<sup>18,19</sup> Physical inactivity, dietary imbalances, and increasing obesity amplify this (fig 1).<sup>20,21</sup>

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.<sup>10</sup> 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.<sup>22</sup> Further work is needed to define mechanisms for this excess cardiovascular disease risk. The risk factors vary by socio-economic 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

## KEY MESSAGES

South Asians are more likely than other ethnicities to develop diabetes, cardiovascular disease, and chronic kidney disease, and these often have an earlier onset and poor outcomes

Strategies for early diagnosis and treatment including awareness generation, opportunistic screening, availability of low cost drugs, and task shifting to health workers must be prioritised

Countries must consider taxation on unhealthy foods, restrictions on advertising, and appropriate food labelling

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

	Bangladesh	India	Nepal	Pakistan	Sri Lanka
<b>Population characteristics</b> <sup>34</sup>					
Population (millions)	161.9	1311.0	28.5	189.0	21.0
Rural population, %	65.7	67.3	81.4	61.2	81.6
Life expectancy at birth, years	71.6	68	69.6	66.2	74.8
Population living on <\$3.10/day PPP, %	NA	58.1	48.3	45.0	14.0
Overweight/obese (BMI ≥25; ≥18 years), age standardised %	18.1	22.0	18.0	23.0	25.2
Hypertension (≥18 years), age standardised %	25.7	25.4	26.4	26.6	21.2
Diabetes, age standardised %	9.2	8.3	9.5	12.1	7.6
<b>Age standardised CVD and diabetes death rates</b> <sup>5</sup>					
CVD death rate per 100 000	363.9	352.6	295.2	530.9	239.9
CVD death rate, % of total deaths	36.5	30.4	29.6	44	38.0
Ischaemic heart disease, % of all deaths in 2015	15.9	17.6	17.4	28.4	20.8
Stroke, % of all deaths in 2015	18.3	8.9	8.8	11.6	12.8
Diabetes death rate per 100 000 in 2015	671	43.3	35.7	53	50.9
Diabetes death rate, % of total deaths	6.7	3.7	3.6	4.4	8.1

BMI=body mass index; CVD=cardiovascular disease; PPP=purchasing power parity.

**Table 2 | Age standardised deaths from chronic kidney disease (CKD) and major attributable risk factors in South Asia<sup>3</sup>**

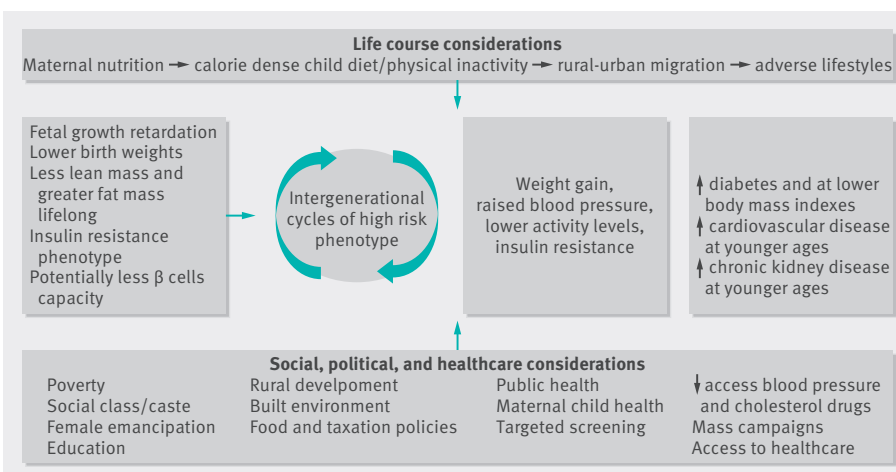
	Bangladesh	India	Pakistan	Nepal	Sri Lanka
<b>Age standardised CKD death rate</b> <sup>5</sup>					
Rate per 100 000	21.78	38.87	18.66	24.27	22.54
% of total deaths	2.2	3.4	1.6	2.4	3.6
<b>Risk factor attributions for CKD</b>					
Systolic blood pressure, %	67.4	69.4	70.5	73.9	83.1
Fasting blood glucose, %	54.4	59.4	56.1	54.5	47.8
High body mass index, %	11.0	14.5	23.7	16.6	18.6

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,<sup>29 30</sup> 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.<sup>31</sup> 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.<sup>32-34</sup> The situation is much worse in rural areas, where an acute event is more likely to be fatal.<sup>31 35</sup>

### 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 expenditure varies 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).<sup>36</sup> 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.



**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; CKD=chronic kidney disease

rapid  $\beta$  cell failure.<sup>2</sup> They may progress more rapidly from a state of high risk of diabetes to frank diabetes and may have accelerated microvascular damage, with evidence of earlier diabetic nephropathy and retinopathy.<sup>2</sup>

### Effects of poor and inconsistent treatment

Significant treatment gaps exist in South Asian populations. Studies report that less

than half of all people with hypertension have received a diagnosis or treatment and less than a third have their blood pressure controlled with drugs.<sup>23-25</sup> The rates of diabetes awareness (50%), glycaemic control (<30%), and chronic kidney disease awareness (<15%) are suboptimal.<sup>24-28</sup>

Delay or prevention of diabetes in South Asians will require earlier intervention—that

**Table 3 | Characteristics of health systems and policies for management of cardiovascular diseases and diabetes in South Asia**

	Bangladesh	India	Nepal	Pakistan	Sri Lanka
<b>Healthcare system</b>					
Health expenditure per capita PPP, \$Int	88.1	267.4	137.4	129	369.2
Health expenditure as % of GDP	2.8	4.7	5.8	2.6	3.5
<b>NCDs in local healthcare infrastructure<sup>a</sup></b>					
Surveillance and monitoring of NCDs or risk factors	Mostly ad hoc sub-national surveys; nationally representative surveillance conducted in 2011 (none since then)	Mostly ad hoc sub-national surveys	Nationally representative surveillance conducted in 2013; no serial monitoring	Mostly ad hoc sub-national surveys; nationally representative surveillance conducted during 1990-94 (none since then)	Mostly ad hoc sub-national surveys
NCD unit or department. in Ministry of Health (as of 2013)	Yes	Yes	Not known	Yes (tobacco control unit only)	Yes
Existence of operational policy/strategy/action plan for CVD (as of 2013)	Yes	Yes	No	No	Yes
National/provincial NCD policy	National Communication and Action Plan for reducing NCD high risk behaviours 2014-16	National Programme For Prevention and Control of Cancer, Diabetes, Cardiovascular Disease and Stroke	Multi-sectoral Action Plan for the Prevention and Control of Non-Communicable Diseases (2014-20)	National Action Plan for Prevention and Control of Non-Communicable Diseases and Health Promotion in Pakistan 2004	National policy and strategic framework for prevention and control of chronic non-communicable diseases 2009
Local hypertension treatment guidelines	No local guidelines	2013 Indian guidelines on hypertension by the Association of Physicians of India	No local guidelines	Pakistan Hypertension League 1998	Health Sector Development Project 2007
Local diabetes management guidelines	Guidelines for care of type 2 diabetes in Bangladesh 2003	Indian Council of Medical Research guidelines for management of type 2 diabetes, 2005	No local guidelines	No local guidelines	Ministry of Sri Lanka diabetes management guidelines, 2011
NCD as line item in health budget	Not as main line item; however, recent addition in other programme categories				Yes, as main line item since 2011

CVD=cardiovascular disease; GDP=gross domestic product; NCD=non-communicable diseases; PPP=purchasing power parity.

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.<sup>31</sup> A model of opportunistic screening for diabetes in patients with tuberculosis is being evaluated in Sri Lanka.<sup>37</sup> 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,<sup>38</sup> 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.<sup>39</sup> In Mexico, an excise tax of 10% on sugar sweetened drinks decreased consumption by an average of 6% over one year.<sup>40</sup> The Indian state of Kerala recently announced a "fat tax" on pizzas, burgers, sandwiches, and tacos sold through branded food outlets.<sup>41</sup> 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).<sup>42</sup> 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 through substitution of palm oil with soya oil.<sup>43</sup> This reduction in cholesterol and low density lipoprotein cholesterol would equate to a 22% lower risk for cardiovascular disease, a huge effect by any standards.<sup>44</sup>

### 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.<sup>34</sup> 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.<sup>45-47</sup> 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.<sup>48</sup>

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.<sup>49</sup> 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.<sup>50</sup> Health insurance reforms must provide for screening and primary care for these conditions to reduce out of pocket expenditure.<sup>51</sup>

Evidence is growing for m-health (mobile health technologies) interventions in improving adherence to treatment, maintaining appointments, data collection, and supporting health workers.<sup>52</sup> More than 80% of the population of South Asia have mobile phones, and a large majority of villages are connected with mobile technology.<sup>53</sup> 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.<sup>54 55</sup>

### 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.<sup>56 57</sup>

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.<sup>58</sup> 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/](http://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.<sup>59</sup> All South Asian countries must institutionalise 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.

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