GLOBAL BURDEN OF CARDIOVASCULAR DISEASE

Perspectives on the management of coronary artery disease in India

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The most striking feature of the management of patients with cardiovascular disease (CVD) in India, is its heterogeneity: from patients treated at tertiary and teaching hospitals, who receive the best possible evidence-based care, to patients who have poor or, even no, access to specialist care and whose condition, therefore, is poorly treated. The challenge for Indian healthcare lies in righting this imbalance. One step in this direction would be to document practice patterns in representative treating hospitals in different regions of the country, to identify the strengths and weaknesses of the system. Resource-sensitive guidelines incorporating evidence-based, cost-effective treatments should be widely disseminated. Large-scale efforts to improve general awareness about CVD and its risk factors, and to promote healthy lifestyles, should be undertaken, and the consumption of tobacco products and unhealthy foods discouraged.

The magnitude of the cardiovascular disease (CVD) epidemic in India and other low-income countries has only recently attracted global attention.[1] Cardiovascular disease is currently the leading cause of death in both urban and rural India. In a study from Chennai city, more than 38% of all deaths were attributable to vascular disease.[2] Similarly, in a survey of 45 villages in the southern Indian state of Andhra Pradesh, diseases of the circulatory system were found to be the leading cause of mortality, accounting for 32% of all deaths.[3] This parallels the six- to eightfold increase in the prevalence of CVD in both urban and rural India seen over the past 40 years.[4] Because of flaws in the methodology adopted, in the studies documenting this increase, doubts have been raised about the veracity of these claims.[5] Nevertheless, recent, more rigorous analyses have also clearly pointed to an increase in the prevalence of CVD and CVD-related mortality.[2 3 6] Further, projections also estimate a more than twofold increase in CVD mortality by 2020, over the rates seen in 1990.[7] Studies by the National Commission for Macroeconomics and Health, Government of India, suggest that the number of patients with coronary artery disease is set to increase to over 60 million by 2015, which would represent about 7.6% of the adult population.[8]

The economic impact of this burgeoning epidemic has recently been estimated.[9] In 2005, the estimated loss of national income due to heart disease, stroke and diabetes was $9 billion for India. This is projected to increase to $54 billion in the year 2015, accounting for a loss of 1.27% of the GDP. In the absence of health insurance for the vast majority of the population, families incur high out-of-pocket spending for illness and hospitalisation. The WHO estimates that of the total spending on healthcare in the country in 2000, 82% was out-of-pocket spending on primary and inpatient care, with only 18% of the costs borne by the Government or third parties.[10] Data from the CREATE Registry of over 20 000 subjects with acute coronary syndromes (ACS) showed that over 75% of patients presenting with ACS paid themselves for their treatment (unpublished data). The economic burden of providing for major health expenditure results in intangible losses to individuals and families and causes a significant proportion of families to slip below the poverty line.[11]

Clearly, there is a need for concerted efforts directed at prevention and effective treatment of CVD. In this article we attempt to provide a perspective on the current management of coronary artery disease in India. For the purpose of this paper, we categorise patients with coronary artery disease into those presenting with acute chest pain syndromes (including both ST elevation and non-ST elevation myocardial infarction and unstable angina) and those presenting with chronic stable angina.

GENERAL COMMENTS

There is a paucity of systematically collected national data on the treatment of coronary artery disease in India. Most information is from secondary and tertiary care hospitals in various parts of the country. Because of the ethnic, economic and cultural diversity, and the differing levels of literacy and awareness among the population, wide variations in health-seeking behaviour, access to healthcare and standards of healthcare are to be expected in different regions of the country. Therefore, extrapolation of the conclusions drawn from the available data to all regions may not be entirely valid.

In addition, there are no satisfactory context-specific, resource-sensitive guidelines to assist doctors in choosing appropriate treatments for their patients. Further, in the absence of

Abbreviations: ACS, acute coronary syndromes; CABG, coronary artery bypass grafting; CVD, cardiovascular disease; ICERs, incremental cost-effectiveness ratios; PCI, percutaneous coronary intervention; STEMI, ST elevation myocardial infarction

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mandatory continuing education for doctors, representatives from the drug and device industry are likely to influence practice patterns.

MANAGEMENT OF ACUTE CHEST PAIN SYNDROMES

Important determinants of the effective treatment of acute chest pain syndromes are the pain-to-door and door-to-drug times. The time from symptom onset to hospital arrival is influenced by several factors, some of which are unique to less developed countries. Because of the time-sensitive nature of the treatments for acute chest pain syndromes, an understanding of these factors and the impact they have on time to presentation is crucial.

Pre-hospital concerns in acute myocardial infarction

Time from symptom onset to presentation at hospital is typically longer among patients in India than in the West.[12–16] The time from symptom onset to emergency department arrival for patients with acute ST elevation myocardial infarction (STEMI) ranges between 110 and 140 minutes in North America,[12 13] while in India, it is 180–330 minutes.[14–16] In the recently concluded CREATE registry, the median symptom-to-door time was 300 minutes for patients with STEMI (unpublished data). This delay in presentation is due to several factors, including lack of symptom awareness, longer distances travelled to reach hospital and problems of transportation.[14 16] Only 5.4% of patients are brought to hospital in an ambulance, with the large majority using public transport (buses) and hired vehicles (taxis, autorickshaws, etc).[14] Of interest, consultation with the family doctor, local practitioner or local primary health centre has been found to be an important cause of delay.[14–16] In addition, older people and women have been observed to present disproportionately late, irrespective of whether their symptoms were typical or atypical.[14 15] Although simple community interventions, directed specifically towards many of the factors cited earlier, can be expected to reduce delays, the delays are probably also the result of deep rooted social imbalances, and may require more than just public health campaigns to effect a favourable change.

In-hospital care

Type of hospital

Because of wide variations in treatment practices, in-hospital care is determined by the type of hospital that the patient attends. In prospectively collected data from 14 hospitals in three southern Indian states, George and colleagues found that government hospitals were least likely to follow guidelines for the treatment of acute STEMI compared with private hospitals or those run by voluntary organisations.[17] Patients treated at hospitals affiliated to medical colleges were more likely to receive fibrinolytic treatment and β blockers than those admitted to non-teaching hospitals.

Treatment of STEMI

In the study by George and colleagues, the rates of adherence to recommended treatments were good. Over 95% of patients received aspirin and 80.5% of eligible patients received fibrinolytic treatment. Nearly 40% of patients received angiotensin converting enzyme inhibitors (ACE-I) and the treatment was carried out according to recommendations in nearly all patients. Similarly, over 47% of patients received β blockers and treatment guidelines were followed in 78% of patients.[17] The in-hospital mortality among the 1072 patients studied was 13.6% and the mean hospital stay was 7 days. A comparison of practice patterns between two tertiary hospitals in India and Canada also showed similar, appropriate rates of usage of standard treatments.[13] In fact, the median door-to-needle time in the Indian hospital was significantly shorter than in the Canadian hospital at that time (30 minutes vs 70.5 minutes). Similarly, the median door-to-needle time in the CREATE registry was 50 minutes (unpublished data).

While this degree of adherence to recommended practice is heartening, it must be noted that these data are from a select set of hospitals in the better developed states of India, and might not be entirely representative of practice patterns across all hospitals. However, a similar high adherence to aspirin (97%), β blockers (66%), ACE inhibitors (73%), lipid-lowering treatment (67%), and reperfusion treatment (79%), was also seen in the recently reported CREATE trial, which included a larger and more representative set of hospitals from across the country.[18] The 30-day mortality rate was 11.3% in the control arm of the trial. Adherence to evidence-based treatments was not restricted only to the patients in the trial, but was also found among patients enrolled in the CREATE Registry (unpublished data). Although these data are indicative of a culture of evidence-based clinical practice, definitive conclusions on hospital performance and in-hospital care cannot be confidently made in the absence of systematic measurement of core process measures (such as, hospital-level, risk-standardised, 30-day mortality rates for assessing the treatment of STEMI) across the spectrum of treating hospitals.

About 6% of patients in India undergo primary angioplasty for STEMI.[18] Primary percutaneous coronary intervention (PCI) is not a feasible first option for reperfusion treatment in India for several reasons. First, the cost of primary angioplasty ranges between 20 and 30 times the cost of streptokinase (which is the most commonly used fibrinolytic agent), depending on the type of treating facility. Second, as of 2004, there were only 220 hospitals capable of performing PCI in the country, with the large majority of them clustered around six major cities. In the absence of reliable, efficient transport services, transport to these centres cannot be achieved within the window of 3–4 hours in most cases. Therefore, primary PCI is financially and geographically inaccessible to most patients with STEMI.

After myocardial infarction, about a fifth of patients underwent coronary angiography, 8.1% angioplasty and 2%, coronary artery bypass surgery within the first month, in the CREATE Registry. Lower rates of an invasive management strategy can largely be accounted for by the fact that over 70% of the patients in this registry were either poor or belonged to lower–middle-income groups (unpublished data). The average cost of angioplasty with bare metal stenting in India is three to four times the average annual income of poor families.

Treatment of ACS (unstable angina and NSTEMI)

Among patients admitted to hospital with non-ST elevation ACS, data from the OASIS 2 Registry suggest that practice patterns are comparable to those in developed countries (countries of the OASIS 1 Registry), except for differences in the rates of heparin use (71.5% in India vs 99.5% in high-income countries) and in the rates of angiography at 7 days (31% vs 39%).[19] Perhaps, these differences, combined with the larger proportion of people with diabetes (39.1% vs 21.3% in high-income countries), and the significantly delayed time to presentation (12 hours vs 8.2 hours), explain the higher event rates seen at 2 years. The proportion of patients who were dead at 2 years was significantly higher in India (15%) than that in the OASIS 1 countries (12.2%). The rates of the composite of death, myocardial infarction or refractory angina were also similarly higher among patients in India. Stroke rates were however significantly lower (0.7% vs 3.0%), probably reflecting the younger age of these patients and the lower rates of angiography and PCI.[19] A higher (85.5%), though not optimal use of antithrombotic drug treatment was found in the CREATE Registry, with low 30-day event rates (death 3.9%) (unpublished data). It may be noted that while the hospitals

participating in the OASIS 2 Registry were mainly tertiary care hospitals, the CREATE Registry had a larger representation of secondary care hospitals. Strategies directed at increasing the use of antithrombotic drug treatment (unfractionated/low molecular weight heparin) might therefore have the potential to improve outcomes.

Specific patient characteristics

Although conventional risk factors account for as much of the risk of developing STEMI among Indian patients as in any other patient population,[20] Indian patients are typically 5 years younger,[21] are more likely to be diabetic[19 21] and are likely to have more risk factors at a younger age.[21] Smoking and dyslipidaemia (apo-B100/apoA-1 ratio) are perhaps the most important of the risk factors that lend themselves to modification. In the INTERHEART Study, lipid abnormalities and current smoking carried the greatest population-attributable risk for STEMI.[20 21] The population-attributable risk for smoking alone climbed to over 58% among young male current smokers (aged <40 years).[22] Forms of tobacco use other than cigarette smoking are prevalent among Indians. These include smoking *beedies* and chewing *paan*. A small amount of tobacco is wrapped in dried temburini leaves and sold as *beedies*. *Paan* is a chewable form of tobacco preparation that is used with limestone paste, areca nut or a betel quid. The association of STEMI with these forms of smoking is just as strong as that with cigarette smoking.[22 23] This highlights the potential for large reductions in rates of STEMI, particularly among young people, and the need for aggressive interventions directed at smoking cessation, particularly during the in-hospital management phase. Smoking cessation interventions are currently only rarely used in Indian hospitals.

Assessing and improving quality of care

There have been few systematic attempts to evaluate the process of care of patients arriving at hospital with a diagnosis of acute chest pain syndromes. The studies by Anand and colleagues[13] and George and colleagues[14] provide some data on the use of evidence-based treatments in selected urban hospitals in India. However, specific process measures to assess the performance of hospitals, such as those used by the Hospital Quality Alliance in the United States,[24] need to be documented and monitored for objective assessment. Such data are essential for the formulation of treatment guidelines and algorithms, and streamlining the delivery of care. Data from the OASIS[19] and the CREATE Registries will be useful in this regard. Recently, efforts to improve quality of care have been attempted, with remarkable success in some regional hospitals in southern India (Professor K Srinath Reddy, personal communication).

MANAGEMENT OF CHRONIC STABLE CVD

Clustering of risk factors

As discussed earlier, Indians develop CVD at a younger age,[21] have a higher prevalence of type 2 diabetes mellitus and impaired glucose tolerance,[25 26] abdominal obesity and dyslipidaemia characterised by an increased apo-B/apo-A1 ratio.[21 25 26] A high prevalence of all the components of the metabolic syndrome has also been shown among the general population in urban India.[27] This clustering of risk factors in the general population is attributable to rapid urbanisation and the substantial increase in disposable incomes, leading to increased consumption of calorie-dense foods, processed foods and foods with high salt content, in combination with low fruit and vegetable consumption and reduced physical activity. This clustering of risk factors holds important implications for both primary and secondary prevention and makes it vital for doctors to identify and effectively control all of these risk factors, while managing patients presenting with manifestations of CVD.

Drug treatment

Despite the sheer scale of the CVD epidemic in developing countries, proven treatments are underused, resulting in a large burden of potentially avoidable mortality and morbidity.[28] For example, for secondary prevention ACE inhibitors are used by fewer than 20% and statins by less than 10% of the eligible population in these countries.[28] This is despite the fact that many of these drugs are currently off-patent and are either available in generic form or as relatively inexpensive brand formulations in the developing world. There is little data about adherence to guidelines and achievement of recommended treatment targets in the management of individual risk factors. Data from the general population in urban India suggest that the ''rule of halves'' still holds at least in the treatment of hypertension, with only 50% of known hypertensives on any form of treatment and only half of these having adequately controlled blood pressures.[29] Even among industrial workers who have better access to healthcare than the general population, risk factor awareness was found to be low.[30 31] A study from a tertiary care teaching hospital suggested that ''treatment guidelines were followed'' in the treatment of hypertension, but did not provide details of blood pressure control.[32] Extrapolation from the follow-up data from the Indian centres participating in registries and clinical trials of patients with STEMI and ACS suggests a more positive scenario.[18 19] Again, these hospitals may not be representative of the practice patterns in all hospitals across the country. Therefore, to obtain a more complete picture, efforts to collect data on the prevalent treatment patterns of patients with chronic CVD, need to be initiated nationally. Analysis of these patterns would help to formulate practical and effective strategies to optimise care and plan for further research.

Combination pharmacotherapy for secondary prevention

There is considerable evidence to suggest that a strategy of simultaneously modifying multiple risk factors can yield large cumulative reductions in the risk of death and cardiovascular events among both patients with[33] and without cardiovascular disease.[34] The concept of combination pharmacotherapy has particular relevance to Indian patients, who are more likely to have multiple risk factors at a younger age. A recent analysis suggests that combining 81 mg aspirin, 40 mg lovastatin and 10 mg lisinopril with metoprolol 50 mg twice daily, in patients with known CVD aged between 35 and 74 years of age, would reduce the lifetime risk of death from cardiovascular disease from 22–40% to 10–15%.[35] If most eligible patients in India (or any other country) were to receive such treatment, life expectancy could potentially be increased by 2 years.[35]

The ''polypill'' for secondary prevention

Distinct from a strategy of combination pharmacotherapy, combining multiple drugs into single units-of-use packaging may improve patient compliance and outcomes.[36] Although the concept of a single pill is inherently appealing, it has not been validated in clinical practice. Further, a single pill precludes the treating doctor's ability to titrate dosages of the component drugs in response to changes in individual risk factors. Therefore, before advocating the use of a single pill for secondary prevention, data regarding safety and efficacy need to be obtained. Other aspects that need to be studied include the pharmaceutical and biochemical stability of the combination, adherence to treatment, cost and acceptability.[37] Two large international, multicentre studies examining these issues are already underway.

Coronary angioplasty

Angioplasty provides symptom relief in drug-refractory patients with non-acute occlusive coronary disease, but does not improve survival. Because of the resultant difficulty in quantifying benefits, most cost-effectiveness analyses have not evaluated angioplasty. In India, in recent years, the numbers of PCI procedures have rapidly increased as a result of an increase in the number of trained interventionists and hospitals able to use PCI. In 2005, over 56 000 angioplasties were performed, with about 67 000 stent implantations and an alarmingly high proportion of drug-eluting stent usage (54%).[38] This information represents data collated from the 109 participating hospitals in the National Registry of Coronary Interventions. The number of procedures is likely to be larger, as a considerable number of small PCI-capable centres are not represented in the registry. In the absence of national guidelines, the indication and timing of procedures, and the choice of stents, is left largely to the discretion of the treating cardiologist. Privately owned hospitals rely, to a large extent, on the number of procedures performed, for their revenues. In the face of aggressive marketing by device manufacturers, and the obvious financial incentive to these hospitals, evidence from the recent large randomised trials[39 40] is unlikely to affect practice, in the absence of some form of regulation. With procedure volumes having become a popular (but questionable) surrogate for hospital performance, publicly funded hospitals are not free from such influence either.

Economics of secondary prevention

As discussed earlier, most healthcare expenditure in India is met by out-of-pocket spending by patients. Although drug formulations in India are much less expensive than in Europe or in North America, chronic, and often lifelong treatment entails considerable economic burden. Further, performance of angioplasty and stenting or coronary artery bypass grafting (CABG), adds greatly to the cost of treatment. Few studies have been done in developing countries analysing the cost effectiveness of treatments used in the management of CVD. Estimates of cost-effectiveness ratios have been extrapolated from data from developed countries with changes in key input prices. But because of differing incomes, drug prices, doctor fees and cost of investigations, there can be no uniform definition of what is cost effective in all countries. The World Health Organization (WHO) Commission on Macroeconomics and Health recommends choosing interventions that are less than three times a country's gross national income per capita.[41]

Incremental cost-effectiveness ratios (ICERs), the incremental cost in dollars per disability-adjusted life year averted, have been calculated for the four most commonly used classes of drugs, and CABG surgery, in the treatment of patients with known CVD.[42] For the South Asian region, the combination of aspirin and a β blocker (atenolol) was found to be cost saving and the addition of enalapril and lovastatin incurred ICERs of $715 and $1819, respectively. At a per capita gross national income of $720, these treatments could therefore be considered cost effective for India. The ICER associated with CABG was considerably greater at $24 040. Gupta and colleagues calculated the median annual retail cost of aspirin (150 mg), ramipril (5 mg), atenolol (50 mg) and atorvastatin (10 mg) to be about 5329 Indian rupees (about $130).[43] In the analysis by Gaziano and colleagues,[35] the use of combination treatment in the South Asian region was associated with ICERs of $300 per quality-adjusted life year, which is well below the threshold for cost effectiveness suggested by the WHO. It has been estimated that such a multidrug regimen could be implemented in India for less than $32 a year. This would increase healthcare expenditure per head by 1.8% ($0.47) a year and would yield substantial reductions in mortality.[35] Efforts should therefore be made to increase the proportion of eligible patients who are treated with these four classes of drugs.

Cardiac rehabilitation

Little is known about the specific issues and concerns arising in the rehabilitation of patients after ACS. There are few dedicated cardiac rehabilitation programmes in the country, reflecting the low priority accorded to this aspect of coronary artery disease management. Data from studies of South Asian immigrants in the UK suggest that these populations are less likely to work towards traditional risk factor modification.[44] These studies also suggest that there may be cultural barriers to lifestyle change among these populations.[45 46] Although extrapolations of these assumptions to people in India might not be entirely appropriate, these data definitely highlight the need for culture-specific rehabilitation programmes which take into account the attitudes and concerns of Indian patients with coronary artery disease.

CONCLUSIONS AND FUTURE DIRECTIONS

The most striking feature of the management of patients with CVD in India, is its heterogeneity: at one end of the spectrum are patients treated at tertiary and teaching hospitals, who receive the best possible evidence-based care and at the other end are patients who have poor or perhaps, even no access to specialist care and whose condition therefore goes unchronicled and poorly treated. The challenge for Indian healthcare lies in righting this imbalance. One step in this direction would be to effectively document prevalent practice patterns, in representative sets of treating hospitals in different regions of the country, in order to identify the strengths and weaknesses of the system. Multiple regional registries could be collated to build a national database. Resource-sensitive guidelines incorporating evidence-based, cost-effective treatments should be formulated and widely disseminated. Combination pharmacotherapy is one strategy which if implemented aggressively among patients with known CVD is likely to yield important gains at little additional cost. Efforts to improve general awareness about CVD and its risk factors and to promote healthy lifestyle practices should be undertaken on a large scale. This must be accompanied by policy level changes aimed at discouraging the consumption of tobacco products and unhealthy foods.

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REFERENCES

1 **Reddy KS**. Cardiovascular diseases in non-Western countries. *N Engl J Med* 2004;**350**:2438–40.
2 **Gajalakshmi V**, Peto R. Verbal autopsy of 80,000 adult deaths in Tamilnadu, south India. *BMC Public Health* 2004;**4**:47.
3 **Joshi R**, Cardona M, Iyengar S, *et al*. Chronic diseases now a leading cause of death in rural India—mortality data from the Andhra Pradesh Rural Health Initiative. *Int J Epidemiol* 2006;**35**:1522–9.
4 **Bahl VK**, Prabhakaran D, Karthikeyan G. Coronary artery disease in Indians. *Indian Heart J* 2001;**53**:707–13.
5 **Ahmad N**, Bhopal R. Is coronary heart disease rising in India? A systematic review based on ECG defined coronary heart disease. *Heart* 2005;**91**:719–25.
6 **Lopez AD**, Mathers CD, Ezzati M, *et al*. Global and regional burden of disease and risk factors, 2001: systematic analysis of population health data. *Lancet* 2006;**367**:1747–57.
7 **Murray CJL**, Lopez AD. *The global burden of disease: a comprehensive assessment of mortality and disability from diseases, injuries, and risk factors in*

1990 and projected to 2020, Cambridge, Mass. : Harvard University Press, 1996.
8 **Indrayan A**. *Forecasting cardiovascular disease cases and associated mortality in India*. New Delhi: National Commission for Macroeconomics and Health, Government of India, 2004.
9 **Abegunde D**, Stanciole A. *An estimation of the economic impact of chronic noncommunicable diseases in selected countries*, World Health Organization. Geneva 2006. Available at http://www.who.int/entity/chp/working_paper_growth%20model29may.pdf (accessed 18 August 2007).
10 **WHO**. *The World Health Report 2000—Health systems: improving performance*. Geneva: WHO, 2000.
11 **Suhrcke M**, Nugent RA, Stuckler D, *et al. Chronic disease: an economic perspective*. London: Oxford Health Alliance, 2006, Available at http://www.oxha.org/initiatives/economics/chronic-disease-an-economic-perspective (accessed 18 August, 2007).
12 **Luepker RV**, Raczynski JM, Osganian S, *et al.* Effect of a community intervention on patient delay and emergency medical service use in acute coronary heart disease: The Rapid Early Action for Coronary Treatment (REACT) Trial. *JAMA* 2000;**284**:60–7.
13 **Anand SS**, Pais P, Pogue J, *et al.* A comparison of practice patterns for acute myocardial infarction between hospitals in Canada and India. *Indian Heart J* 1997;**49**:35–41.
14 **George E**, Savitha D, Pais P. Pre-hospital issues in acute myocardial infarction. *J Assoc Physicians India* 2001;**49**:320–3.
15 **Rajagopalan RE**, Chandrasekaran S, Pai M, *et al.* Pre-hospital delay in acute myocardial infarction in an urban Indian hospital: a prospective study. *Natl Med J India* 2001;**14**:8–12.
16 **Malhotra S**, Gupta M, Chandra KK, *et al.* Prehospital delay in patients hospitalized with acute myocardial infarction in the emergency unit of a north Indian tertiary care hospital. *Indian Heart J* 2003;**55**:349–53.
17 **George E**, Hunsberger, Savitha D, et al. Treatment of acute myocardial infarction: Does the type of hospital make a difference? *Indian Heart J* 1999;**51**:161–6.
18 **Yusuf S**, Mehta SR, Xie C, *et al.* CREATE Trial Group Investigators. Effects of reviparin, a low-molecular-weight heparin, on mortality, reinfarction, and strokes in patients with acute myocardial infarction presenting with ST-segment elevation. *JAMA* 2005;**293**:427–35.
19 **Prabhakaran D**, Yusuf S, Mehta S, *et al.* Two-year outcomes in patients admitted with non-ST elevation acute coronary syndrome: results of the OASIS Registry 1 and 2. *Indian Heart J* 2005;**57**:217–25.
20 **Yusuf S**, Hawken S, Ounpuu S, *et al.* INTERHEART Study Investigators. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART Study): case-control study. *Lancet* 2004;**364**:937–52.
21 **Joshi P**, Islam S, Pais P, *et al.* Risk factors for early myocardial infarction in South Asians compared with individuals in other countries. *JAMA* 2007;**297**:286–94.
22 **Teo KK**, Ounpuu S, Hawken S, *et al.* INTERHEART Study Investigators. Tobacco use and risk of myocardial infarction in 52 countries in the INTERHEART study: a case-control study. *Lancet* 2006;**368**:647–58.
23 **Pais P**, Fay MP, Yusuf S. Increased risk of acute myocardial infarction associated with beedi and cigarette smoking in Indians: final report on tobacco risks from a case-control study. *Indian Heart J* 2001;**53**:731–5.
24 **Bradley EH**, Herrin J, Elbel B, *et al.* Hospital quality for acute myocardial infarction: correlation among process measures and relationship with short-term mortality. *JAMA* 2006;**296**:72–8.
25 **Yusuf S**, Reddy S, Ounpuu S, *et al.* Global burden of cardiovascular diseases: Part II: Variations in cardiovascular disease by specific ethnic groups and geographic regions and prevention strategies. *Circulation* 2001;**104**:2855–64.
26 **Mohan V**, Deepa R, Rani SS, *et al.* Chennai Urban Population Study (CUPS No 5). Prevalence of coronary artery disease and its relationship to lipids in a selected population in South India: the Chennai Urban Population Study (CUPS No 5). *J Am Coll Cardiol* 2001;**38**:682–7.
27 **Deepa M**, Farooq S, Datta M, *et al.* Prevalence of metabolic syndrome using WHO, ATPIII and IDF definitions in Asian Indians: the Chennai Urban Rural Epidemiology Study (CURES-34). *Diabetes Metab Res Rev* 2007;**23**:127–34.
28 **Mendis S**, Abegunde D, Yusuf S, *et al.* WHO study on Prevention and REcurrences of Myocardial Infarction and StrokE (WHO-PREMISE). *Bull World Health Organ* 2005;**83**:820–8.
29 **Deepa R**, Shanthirani CS, Pradeepa R, *et al.* Is the 'rule of halves' in hypertension still valid?—Evidence from the Chennai Urban Population Study. *J Assoc Physicians India* 2003;**51**:153–7.
30 **Reddy KS**, Prabhakaran D, Chaturvedi V, *et al.* Methods for establishing a surveillance system for cardiovascular diseases in Indian industrial populations. *Bull World Health Organ* 2006;**84**:461–9.
31 **Prabhakaran D**, Shah P, Chaturvedi V, *et al.* Cardiovascular risk factor prevalence among men in a large industry of northern India. *Natl Med J India* 2005;**18**:59–65.
32 **Malhotra S**, Karan RS, Pandhi P, *et al.* Pattern of use and pharmacoeconomic impact of antihypertensive drugs in a north Indian referral hospital. *Eur J Clin Pharmacol* 2001;**57**:535–40.
33 **Yusuf S**. Two decades of progress in preventing vascular disease. *Lancet* 2002;**360**:2–3.
34 **Wald NJ**, Law MR. A strategy to reduce cardiovascular disease by more than 80%. *BMJ* 2003;**326**:1419–24.
35 **Gaziano TA**, Opie LH, Weinstein MC. Cardiovascular disease prevention with a multidrug regimen in the developing world: a cost-effectiveness analysis. *Lancet* 2006;**368**:679–86.
36 **Connor J**, Rafter N, Rodgers A. Do fixed-dose combination pills or unit-of-use packaging improve adherence? A systematic review. *Bull World Health Organ* 2004;**82**:935–9.
37 **Xavier D**, Devereaux PJ, Goyal A, *et al.* Polypharmacotherapy for primary prevention of cardiovascular disease. *Indian Heart J* (in press).
38 **Kodungati SC**. Coronary intervention data in India for the year 2005. *Indian Heart J* 2006;**58**:282–4.
39 **Hochman JS**, Lamas GA, Buller CE, *et al.* Coronary intervention for persistent occlusion after myocardial infarction. *N Engl J Med* 2006;**355**:2395–407.
40 **Boden WE**, O'Rourke RA, Teo KK, *et al.* Optimal medical therapy with or without PCI for stable coronary disease. *N Engl J Med* 2007;**356**:1503–16.
41 **World Health Organization**. *Macroeconomics and health: investing in health for economic development—report of the Commission on Macroeconomics and Health*. Geneva: WHO, 2001.
42 **Gaziano TA**, Reddy KS, Paccaud F, *et al. Cardiovascular disease. Disease control priorities in developing countries*, 2nd ed. New York: Oxford University Press, 2006:645–662.
43 **Gupta R**, Prakash H, Gupta RR. Economic issues in coronary heart disease prevention in India. *J Hum Hypertens* 2005;**19**:655–7.
44 **Lip GY**, Luscombe C, McCarry M, *et al.* Ethnic differences in public health awareness, health perceptions and physical exercise: implications for heart disease prevention. *Ethn Health* 1996;**1**:47–53.
45 **Farooqi A**, Nagra D, Edgar T, *et al.* Attitudes to lifestyle risk factors for coronary heart disease amongst South Asians in Leicester: a focus group study. *Fam Pract* 2000;**17**:293–7.
46 **Webster RA**, Thompson DR, Mayou RA. The experiences and needs of Gujarati Hindu patients and partners in the first month after a myocardial infarction. *Eur J Cardiovasc Nurs* 2002;**1**:69–76.