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Heart failure: Epidemiology and prevention in India

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Abstract

Reliable estimates of heart failure are lacking in India because of the absence of a surveillance programme to track incidence, prevalence, outcomes and key causes of heart failure. Nevertheless, we propose that the incidence and prevalence rates of heart failure are rising due to population, epidemiological and health transitions. Based on disease-specific estimates of prevalence and incidence rates of heart failure, we conservatively estimate the prevalence of heart failure in India due to coronary heart disease, hypertension, obesity, diabetes and rheumatic heart disease to range from 1.3 to 4.6 million, with an annual incidence of 491 600–1.8 million. The double burden of rising cardiovascular risk factors and persistent 'pre-transition' diseases such as rheumatic heart disease, limited healthcare infrastructure and social disparities contribute to these estimates. Staging of heart failure, introduced in 2005, provides a framework to target preventive strategies in patients at risk for heart failure (stage A), with structural disease alone (B), with heart failure symptoms (C) and with end-stage disease (D). Policy-level interventions, such as regulations to limit salt and tobacco consumption, are effective for primordial prevention and would have a wider impact on prevention of heart failure. Clinical preventive interventions and clinical quality improvement interventions, such as treatment of hypertension, atherosclerotic disease, diabetes and acute decompensated heart failure are effective for primary, secondary and even tertiary prevention.

BACKGROUND

The incidence and prevalence estimates of heart failure (HF) are unreliable in India because of the lack of surveillance systems to adequately capture these data. This lack of HF surveillance is not unique to India. In 2001, Mendez and Cowie found no population-based HF studies in all developing countries,[1] making global prevalence estimates difficult. Estimating the burden of HF is further hampered by the lack of a standard definition. In fact, the WHO Global Burden of Disease study places HF in several categories within cardiovascular disease, including ischaemic, hypertensive, inflammatory and rheumatic heart disease (RHD).[2]

The epidemiology of HF in India has likely changed from that reported in 1949 by Vakil, describing hypertension-coronary (31%), RHD (29%), syphilis (12%), and pulmonary (9%) as the primary causes in 1281 patients hospitalized due to HF.[3] More recent evaluations have provided limited insight into the broader HF landscape in India, since these have focused on specific aetiologies of HF (such as HF caused by endomyocardial fibrosis[4] and ST-segment elevation myocardial infarction),[5,6] and HF outcomes in select patients with systolic dysfunction in tertiary care centres,[7] rather than community-based surveillance.

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The prevalence of HF in India is possibly on the rise as India remains doubly burdened by the rise in the risk factors of traditional cardiovascular disease (CVD) and by the persistence of pre-transitional diseases such as RHD, endomyocardial fibrosis, tuberculous pericardial disease and anaemia. Prevention of HF—a target that can be overlooked in clinical practice—offers several effective opportunities for clinicians and for patients. In this review, we discuss the (i) epidemiology of HF in India today and the potential reasons for this burden, (ii) staging of HF as a paradigm for prevention of HF, as recommended by the American Heart Association/American College of Cardiology heart failure guidelines, and (iii) interventions for prevention of HF in India.

EPIDEMIOLOGY

Transitions

India's economic development, industrialization and urbanization have been accompanied by transitions that contribute to the increase in the overall risk of HF.

First, the population of India is ageing due to recent successes against communicable diseases such that the number of people >60 years old will increase from 62 million in 1996 to 113 million in 2016.[8] HF is predominantly a disease of the elderly, as the lifetime risk for HF increases with age, so the burden of HF is likely to increase with the ageing population.[9] Second, the epidemiological transition reflects changes in disease patterns as societies develop, as first described by Omran in 1971,[10] and amended by Olshansky and Ault in 1986[11] and Yusuf and colleagues in 2005.[12] The 5 ages include: pestilence and famine, receding pandemics, degenerative and man-made diseases, delayed degenerative diseases, and health regression and social upheaval (the age of inactivity and obesity has recently been proposed as an alternate fifth age).[13] India straddles several 'ages' along this spectrum given its uneven development, but appears to be moving towards the age of delayed degenerative diseases in most of the country. These population and epidemiological transitions are finally reflected in the subsequent health transition (Table I), which tracks changes in the health status as populations move from high infant mortality and fertility rates to low infant mortality and fertility rates.

Burden of CVD and risk factors

CVD is currently the leading cause of death in India and its prevalence is projected to rise. In 2000, there were an estimated 30 million people with coronary heart disease (CHD) alone in India, or a nearly 3% prevalence.[8,14] The annual incidence of HF for patients with CHD ranges from 0.4% to 2.3% per year,[15,16] suggesting that 120 000–690 000 Indians could develop symptomatic HF due to CHD every year, assuming none has HF at baseline and the at-risk population does not diminish. After 5 years, the total number of HF patients accrued could range from 600 000 to 3.5 million; with an estimated 50% mortality at 5 years,[17] the prevalence of HF due to CHD alone could be estimated to range from 300 000 to 1.75 million. Nevertheless, as the prevalence of patients with CHD rises, so too will the prevalence of patients with HF.

The prevalence of other risk factors of HF is also rising in India. In addition to the ageing population described above, the prevalence of hypertension is projected to increase from 118 million (2000) to 214 million (2025).[18] If the annual incidence of HF in patients with a systolic blood pressure (SBP) of 144–154 mmHg is 0.1% to 0.6%, as demonstrated in the Hypertension Optimal Treatment (HOT)[19] and United Kingdom Prospective Diabetes Study (UKPDS) trials,[20] respectively, then the number of new HF cases due to hypertension may increase from 118 000–708 000 per year in 2000 to 214 000–1.3 million per year in 2025, conservatively assuming that the bulk of patients with hypertension in India have a SBP in the 144–154 mmHg range. After 5 years of HF incidence based upon year 2000 estimates

for hypertension, the total number of HF patients accrued could range from 590 000 to 3.5 million; with an estimated 50% mortality at 5 years, the prevalence of HF due to hypertension alone could be estimated to range from 295 000 to 1.8 million. However, this possibly represents an underestimate, due to conservative estimates of the prevalence of hypertension, as well as the linear relationship between risk of HF and blood pressure that occurs for values even <140 mmHg.

The annual incidence of HF due to obesity (body mass index [BMI] >30 kg/m^2) has been estimated to increase by 0.3% in women and 0.5% in men, in the Framingham Heart Study, after adjustment for age, hypertension, left ventricular hypertrophy, myocardial infarction, valve disease, diabetes and cholesterol.[21] Few studies in India have used a BMI threshold of 30 kg/m^2, which makes it difficult to accurately estimate the prevalence of obesity. Reddy *et al*. estimated the prevalence of obesity (BMI >30 kg/m^2) in 10 970 participants from urban Delhi and rural Haryana in 2002 to be 6.8%.[22] Using these estimates as a benchmark, a 5% prevalence of obesity (BMI >30 kg/m^2) in India would lead to an estimated 180 000–300 000 cases of HF annually. After 5 years of the incidence of HF based upon 5% obesity prevalence estimates, the total number of HF patients accrued could range from 900 000–1.5 million; with an estimated 50% mortality at 5 years, the prevalence of HF due to obesity alone could be estimated to range from 450 000 to 750 000.

Similarly, the prevalence of diabetes in India is projected to increase from 32 million (2000) to 70 million (2025).[23] The incidence of HF has been demonstrated to increase from 2.3 per 1000 person-years for a HbA1c <6% to 11.9 per 1000 person-years for a HbA1c >11.9%. Taking the estimate of HF incidence based upon optimal glucose control, the annual incidence of HF due to diabetes may increase from 73 600 (2000) to 161 000 (2025). After 5 years of HF incidence based upon the diabetes estimates for the year 2000, the total number of HF patients accrued could be 368 000; with an estimated 50% mortality at 5 years, the prevalence of HF due to diabetes alone could be estimated at 184 000. However, this is likely to be an underestimate, due to conservative estimates of HbA1c.

Unfinished, pre-transition agenda

The unfinished, pre-transition agenda that bookends India's double burden of disease includes a relatively high prevalence of pre-transition diseases, limited healthcare infrastructure, and health disparities, which disproportionately affect people from lower socioeconomic classes and potentially exacerbate disparities further. Prevalence rates for RHD remain high in India, reaching 1.0–5.4 cases per 1000 schoolchildren in one study.[24] Approximately 98 000 people died from RHD in India in 2004,[2] which would add to the total estimated HF prevalence given above. As there is insufficient evidence on the role of secondary prevention of rheumatic fever in preventing the progression of valvular disease in RHD, the risk of HF remains unclear in patients with RHD.[25] Other diseases that can manifest as HF such as endomyocardial fibrosis, tuberculous constrictive pericarditis and infectious endocarditis, appear to be present in greater proportions in India compared with its high-income country counterparts, but data are sparse regarding the prevalence of these diseases in India.

Since patients have uneven and limited access to healthcare in India, the healthcare infrastructure itself may play a role in the rising burden of HF.[26] The public healthcare system is often overloaded, which makes access to basic services difficult. India has <2% penetration of health insurance (government employees are an exception),[27] making the out-of-pocket costs for prevention of HF relatively expensive. Emergency services are not widely available in India, such that patients who experience acute cardiac events, such as acute coronary syndrome (ACS), typically have longer symptom-to-door and door-to-needle

times than in other countries.[28] This combination of inaccessibility, unaffordable treatment and treatment delay possibly increases the incidence of HF in India.

Xavier and colleagues evaluated the association between ACS care and socioeconomic status (SES) in the India-based CREATE ACS registry.[29] Patients with a lower SES were less likely to undergo coronary angiography, percutaneous coronary intervention, and coronary artery bypass graft surgery and were less likely to receive medications for secondary prevention of CHD. These disparities contributed significantly to the 2.7% absolute increase in 30-day mortality seen in the poorest stratum compared with that in the richest stratum. However, these differences in mortality were abolished after adjusting for risk factors of CHD, location of infarct, and treatments, suggesting that uniform distribution of CHD and treatment of risk factors of CHD offers an opportunity to improve care. Important social determinants of health such as poverty, lack of empowerment, and healthcare inequalities[30] impede these efforts and are likely to exacerbate the burden of HF in India.

Taken together, the estimated prevalence of HF due to CHD, hypertension, obesity, diabetes and RHD alone in 2000 ranges from 1.3 million to 4.6 million, with an annual incidence ranging from 491 600 to 1.8 million. Both estimates are projected to rise and do not account for other important causes of HF such as alcoholic, familial, hypertrophic and idiopathic dilated cardiomyopathies, pericardial disease and endomyocardial fibrosis. The estimated prevalence of HF in India remains lower than that in the USA (5.8 million),[17] but the rate for potential increase and subsequent morbidity and mortality strengthens the case for prevention of HF in India.

STAGES OF HEART FAILURE: GOALS

In 2005, the American Heart Association (AHA) and American College of Cardiology (ACC) introduced updated HF clinical practice guidelines that moved beyond the New York Heart Association (NYHA) classification system to include four new stages of HF—A through D.[31]

Stage A represents patients who do not have structural heart disease nor do they have symptoms of HF but are at high risk for developing HF. These patients include those with hypertension, diabetes, atherosclerotic disease, obesity, metabolic syndrome, family history of cardiomyopathy, or exposure to cardiotoxic drugs (e.g. anthracyclines). The primary goals of treating stage A patients include treatment of hypertension and dyslipidaemia, cessation of tobacco, alcohol and illicit drug use, encouragement of exercise and management of metabolic syndrome. Anticholinesterase inhibitors (ACE-I) or angiotensin receptor blockers (ARBs) are recommended for patients with concomitant diabetes and/or vascular disease.

Stage B represents patients with evidence of structural heart disease in the absence of symptoms of HF (such as left ventricular hypertrophy, left ventricular dysfunction or valvular heart disease). The primary goals of treating stage B patients are similar to those for stage A patients. ACE-I or ARBs and beta-blockers are recommended for appropriate patients with left ventricular dysfunction and/or vascular disease, as well as implantable cardioverter defibrillators (ICDs), in selected patients.

Stage C represents patients with a history, symptoms and clinical signs consistent with HF and fall into the NYHA classification system (I–IV). The primary goals of treating stage C patients include all the goals of stages A and B, as well as dietary salt restriction. Aldosterone antagonists, digoxin, hydralazine/nitrate combination therapy, and biventricular pacemaker/ICDs are recommended for selected patients.

Stage D represents patients with advanced HF who have marked symptoms at rest despite maximal medical therapy. These patients are often hospitalized repeatedly and cannot be discharged without specialized therapies. The primary goals of treating stage D patients include all the goals of stages A, B and C, as well as decisions regarding the appropriate level of care. Clinicians and patients in India can use this paradigm to help guide their goals and strategies, particularly in stages A and B patients where prevention of HF is achievable.

INTERVENTIONS FOR PREVENTION IN INDIA

Primordial prevention of HF

Policy-level interventions targeting HF and risk factors for HF could have a major impact on the burden of disease in India through primordial prevention. First, regulations to limit the salt content of foods have a great potential to reduce the burden of hypertension, CHD and subsequent incidence of HF across a wide spectrum of the population. A 2010 study modelling a 3 g reduction in salt intake across the population of USA estimated an annual reduction in myocardial infarction by 54 000–99 000, stroke by 32 000–66 000, and overall mortality by 44 000–92 000.[32] Subsequently the incidence of HF should also decrease, though this was not specifically modelled. Whether reduction of salt intake in India would be safe and effective needs further study.

Second, tobacco taxation that includes *bidis* and smokeless tobacco provides the most powerful tool to immediately reduce consumption of tobacco and helps decrease the overall CVD burden, including HF.[33] *Bidis* and smokeless tobacco account for over 80% of tobacco consumption in India but only 12% of the excise tax.[34] *Bidis* attract little excise tax because they are usually produced by small manufacturers who are dispersed throughout the country; excise duties effectively cover only branded *bidis*.[34] Tobacco taxation has been shown to reduce consumption in high-income countries,[35] but the reductions may be higher in India due to higher price sensitivity of tobacco consumers in India.

Both salt reduction and tobacco control are the two cost-effective strategies for reduction of CVD that are ready for scale-up in countries such as India and should be adopted as quickly as possible.[36] However, to monitor and evaluate any interventions, community-based surveillance of HF and risk factors of HF is required to help clinicians, researchers and policy-makers understand the burden of HF in India more clearly rather than through crude estimates such as those detailed above. Ongoing data collection and monitoring would provide policy-makers with the framework to evaluate the impact of HF- and HF risk factor-associated policy decisions[37] and to appropriately allocate patient care and research funding in a timely, responsive fashion.

Primary prevention

Effective clinical interventions for prevention of HF in asymptomatic patients target the three major, modifiable HF risk factors for stage A patients, namely hypertension, atherosclerotic disease and diabetes. Stage B patients, particularly those with asymptomatic left ventricular dysfunction, represent another group that derive even greater benefit from preventive efforts because of their increased absolute risk. Landmark hypertension trials such as Swedish Trial in Old Patients with Hypertension (STOP),[38] Systolic Hypertension in the Elderly Program (SHEP),[39] and Systolic Hypertension in Europe (Syst-Eur)[40] demonstrated a 1.5%–2.5% absolute risk reduction in the incidence of HF over the 2–4 year follow up period with antihypertensive therapy. The number of patients needed to treat (NNT) to prevent one HF incident event ranged from 40 to 65. The patients had a mean age of ≥70 years in all three trials and a starting mean SBP >170 mmHg, conferring a high short term absolute risk for HF.

Drugs used in these three trials included thiazide diuretics, ACE-I, calcium channel blockers, beta-blockers and reserpine. While the Joint National Commission VII recommends using a thiazide diuretic as the first-line agent for hypertension,[41] ACE-I or ARBs are also recommended for patients with atherosclerotic disease or diabetes by the AHA/ACC.[42] Beta-blockers are typically reserved only for patients who have a history of myocardial infarction or angina.[42,43]

Patients with atherosclerotic disease can also be treated with lipid-lowering therapies to reduce their risk of HF, in addition to decreasing their mortality risk. The Scandinavian Simvastatin Survival Study (4S),[44] Cholesterol And Recurrent Events (CARE),[45] and Long-Term Intervention with Pravastatin in Ischaemic Disease (LIPID)[46] trials all demonstrated reduction in the incidence of HF with statins in patients with atherosclerotic disease. However, the majority of the risk reduction appeared to be mediated via a concomitant reduction in recurrent vascular events such as myocardial infarction, since the relative risk reductions were similar. The NNT to prevent one HF event ranged widely from 31 to 500 in these three trials.

For asymptomatic patients with evidence of structural heart disease (Stage B patients), specifically left ventricular dysfunction, the benefits of preventive therapy are even greater. The Studies of Left Ventricular Dysfunction (SOLVD) prevention arm demonstrated a 9% absolute risk reduction with the use of enalapril in patients with asymptomatic left ventricular dysfunction after 4 years of treatment (NNT=11).[47] Likewise, the Survival and Ventricular Enlargement (SAVE), Acute Infarction Ramipril Efficacy (AIRE) and Trandolapril in Patients with Reduced Left-Ventricular Function after Acute Myocardial Infarction (TRACE) trials studied the effects of ACE-I (enalapril, ramipril and trandolapril) on patients following a myocardial infarction and demonstrated a combined 3.6% absolute risk reduction in the incidence of HF over a median of 31 months (NNT=28).[48] The Carvedilol Post-Infarction Survival Control in Left Ventricular Dysfunction (CAPRICORN) study demonstrated a more modest 2% absolute risk reduction (NNT=50) with carvedilol in the incidence of hospitalization due to HF, but the follow up period was for only 1.3 years.[49] In comparison, the NNT for glycoprotein IIb/IIIa antagonists to prevent one death or myocardial infarction at 30 days ranges from 32 to 250 in patients with unstable angina/non-ST-segment elevation myocardial infarction, depending on the timing of drug administration and concomitant treatment strategy (invasive *v*. non-invasive).[50]

Patients with diabetes can be treated with ramipril to decrease the incidence of HF, as demonstrated in the Heart Outcomes Prevention Evaluation sub-study (MICRO-HOPE).[51] Ramipril decreased the incidence of HF by 2.3% over 5 years (NNT=43), though the risk of severe HF requiring hospitalization was not decreased with ramipril compared with placebo. ARBs have also been shown to decrease the incidence of HF in people with diabetes when compared with beta-blockers,[52] but this difference appears to be mediated through a differential reduction in blood pressure. While observational data have demonstrated a decreased incidence of HF with better glycaemic control, neither the ADVANCE nor the ACCORD studies demonstrated a difference in incidence of HF between the standard and intensive glucose control arms.[53,54]

RHD requires a broader effort targeting primary antibiotic prophylaxis[55] or development of an effective group A streptococcal vaccine[56] to prevent HF, particularly since secondary prevention with penicillin has not been clearly shown to prevent the progression of valvular disease, as previously mentioned.[25] Major reductions in RHD in Cuba[57] and Costa Rica[58] have been demonstrated through comprehensive programmes that increase community awareness of group A streptococcal infections and integrate clinical diagnostics and single dose benzathine penicillin treatment in primary care settings. While this strategy may not be

easy to adopt throughout India, it may be more cost-effective than secondary prevention alone.[59]

Treatment of tuberculosis provides another opportunity to prevent HF, through the prevention of symptoms due to constrictive pericarditis. No studies have evaluated the treatment benefit in the primary prevention of HF, but the advent of antituberculous drugs for treatment of pericardial tuberculosis has been associated with a decline in estimated case fatality rate from nearly 100% to as low as 8%.[60] The forthcoming Investigation of the Management of Pericarditis in Africa (IMPI Africa) Pilot Study should provide further insight into the prevention of HF from tuberculosis.[61] The investigators aim to evaluate the safety of a 6-week course of adjunctive prednisolone which, if positive, will provide preliminary data for a larger trial that will evaluate the efficacy of prednisolone in reducing pericardial complications (death, constriction or tamponade requiring drainage) in tuberculosis patients with pericardial effusions.

Secondary and tertiary prevention of HF through clinical quality improvement

Clinical quality improvement programmes—often organized through professional societies[62]—can help standardize and improve clinical care for patients at risk for asymptomatic HF (stages A and B), as well as those patients with symptomatic HF (stages C and D) to prevent HF and its complications, including hospitalization and death. Participation in practice improvement programmes has been shown to increase use of evidence-based care, adherence to performance measures, and decreased length of stay (for hospitalized HF patients) and may improve clinical outcomes.[63,64]

Appropriately trained and supported non-physician health workers (NPHWs) may be able to play a complementary role in the support and delivery of these programmes in the future.[65] India also currently lacks cardiovascular clinical practice guidelines, as well as nationally representative quality improvement initiatives to improve care for CVD. Development of guidelines and quality improvement programmes through professional societies offers a potential avenue for clinicians and researchers to improve prevention of HF through the establishment and implementation of India-specific practice standards.

CONCLUSION

The burden of HF in India appears high, and estimates of prevalence range from 1.3 million to 4.6 million, with an annual incidence of 491 600–1.8 million. However, reliable data are lacking because of inadequate surveillance systems. Population, epidemiological and health transitions will continue to play an important role in the future burden of HF in India. The formulation of stages of HF (A to D) provides a preventive framework across the spectrum of patients with HF, from at-risk to end-stage. Incorporating effective, comprehensive (primordial through tertiary) prevention of HF provides the best opportunity to curb the projected rise of HF in India.

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References

1. Mendez GF, Cowie MR. The epidemiological features of heart failure in developing countries: A review of the literature. Int J Cardiol. 2001; 80:213–19. [PubMed: 11578717]
2. World Health Organization. Global burden of disease—2004 update. Geneva: Switzerland: 2004.
3. Vakil RJ. A statistical study of 1281 cases of congestive cardiac failure or myocardial insufficiency in India. Indian Physician. 1949; 8:281–9. [PubMed: 18268798]
4. Gupta PN, Valiathan MS, Balakrishnan KG, Kartha CC, Ghosh MK. Clinical course of endomyocardial fibrosis. Br Heart J. 1989; 62:450–4. [PubMed: 2605058]
5. Achari V, Prakash S, Sinha AK, Thakur AK. Short-term mortality and complications in ST elevation myocardial infarction—the Heart Hospital experience. J Indian Med Assoc. 2008; 106:650–4. [PubMed: 19552098]
6. Grover G, Dutta R, Gadpayle AK, Saha S. Changing patterns of cardiovascular risk factors and heart related sickness in relation with acute myocardial infarction in Delhi, India. J Indian Med Assoc. 2009; 107:636–638. 640 passim. [PubMed: 20337244]
7. Ramachandran K, Husain N, Maikhuri R, Seth S, Vij A, Kumar M, et al. Impact of a comprehensive telephone-based disease management programme on quality-of-life in patients with heart failure. Natl Med J India. 2007; 20:67–73. [PubMed: 17802984]
8. National Commission on Population, Government of India. [3 March 2010] Available at http://populationcommission.nic.in/
9. Lloyd-Jones DM, Larson MG, Leip EP, Beiser A, D'Agostino RB, Kannel WB, et al. Lifetime risk for developing congestive heart failure: The Framingham Heart Study. Circulation. 2002; 106:3068–72. [PubMed: 12473553]
10. Omran AR. The epidemiologic transition: A theory of the epidemiology of population change. Milbank Mem Fund Q. 1971; 49:509–38. [PubMed: 5155251]
11. Olshansky SJ, Ault AB. The fourth stage of the epidemiologic transition: The age of delayed degenerative diseases. Milbank Q. 1986; 64:355–91. [PubMed: 3762504]
12. Yusuf S, Ounpuu S, Anand S. The global epidemic of atherosclerotic cardiovascular disease. Med Princ Pract. 2002; 11(Suppl 2):3–8. [PubMed: 12444305]
13. Gaziano, JM. Global burden of cardiovascular disease. In: Libby, P.; Bonow, RO.; Mann, DL.; Zipes, DP., editors. Braunwald's heart disease: A textbook of cardiovascular medicine. 8. New York: Saunders; 2007.
14. Gupta R, Joshi P, Mohan V, Reddy KS, Yusuf S. Epidemiology and causation of coronary heart disease and stroke in India. Heart. 2008; 94:16–26. [PubMed: 18083949]
15. Yusuf S, Sleight P, Pogue J, Bosch J, Davies R, Dagenais G. The Heart Outcomes Prevention Evaluation Study Investigators. Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. N Engl J Med. 2000; 342:145–53. [PubMed: 10639539]
16. Fox KM. European trial on reduction of cardiac events with perindopril in stable coronary artery disease investigators. Efficacy of perindopril in reduction of cardiovascular events among patients with stable coronary artery disease: Randomised, double-blind, placebo-controlled, multicentre trial (the EUROPA study). Lancet. 2003; 362:782–8. [PubMed: 13678872]
17. Lloyd-Jones D, Adams RJ, Brown TM, Carnethon M, Dai S, De Simone G, et al. American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics—2010 update: A report from the American Heart Association. Circulation. 2010; 121:e46–e215. Epub 2009 Dec 17. [PubMed: 20019324]
18. World Health Organization. Geneva:Switzerland: The WHO Global InfoBase. Available at https://who.int/infobase [3 March 2010]
19. Hansson L, Zanchetti A, Carruthers SG, Dahlöf B, Elmfeldt D, Julius S, et al. HOT Study Group. Effects of intensive blood-pressure lowering and low-dose aspirin in patients with hypertension: Principal results of the Hypertension Optimal Treatment (HOT) randomised trial. Lancet. 1998; 351:1755–62. [PubMed: 9635947]
20. Neal B, MacMahon S, Chapman N. Blood Pressure Lowering Treatment Trialists' Collaboration. Effects of ACE inhibitors, calcium antagonists, and other blood-pressure-lowering drugs: Results

of prospectively designed overviews of randomised trials. Lancet. 2000; 356:1955–64. [PubMed: 11130523]

21. Kenchaiah S, Evans JC, Levy D, Wilson PW, Benjamin EJ, Larson MG, et al. Obesity and the risk of heart failure. N Engl J Med. 2002; 347:305–13. [PubMed: 12151467]
22. Reddy KS, Prabhakaran D, Shah P, Shah B. Differences in body mass index and waist: Hip ratios in North Indian rural and urban populations. Obes Rev. 2002; 3:197–202. [PubMed: 12164472]
23. Rodgers A, Ezzati M, Vander Hoorn S, Lopez AD, Lin RB, Murray CJ. Comparative risk assessment collaborating group distribution of major health risks: Findings from the global burden of disease study. PLoS Med. 2004; 1:e27. [PubMed: 15526049]
24. Thakur JS, Negi PC, Ahluwalia SK, Vaidya NK. Epidemiological survey of rheumatic heart disease among school children in the Shimla hills of northern India: Prevalence and risk factors. J Epidemiol Community Health. 1996; 50:62–7. [PubMed: 8762356]
25. Manyemba J, Mayosi BM. Penicillin for secondary prevention of rheumatic fever. Cochrane Database Syst Rev. 2002; 3 CD002227.
26. Ali MK, Narayan KM, Mohan V. Innovative research for equitable diabetes care in India. Diabetes Res Clin Pract. 2009; 86:155–67. [PubMed: 19796835]
27. WHO. Coping with health care costs: Implications for the measurement of catastrophic expenditures and poverty: Health system performance assessment. Geneva: World Health Organization; 2003.
28. Prabhakaran D, Yusuf S, Mehta S, Pogue J, Avezum A, Budaj A, 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. [PubMed: 16196178]
29. Xavier D, Pais P, Devereaux PJ, Xie C, Prabhakaran D, Reddy KS, et al. Treatment and outcomes of acute coronary syndromes in India (CREATE): A prospective analysis of registry data. Lancet. 2008; 371:1435–42. [PubMed: 18440425]
30. Commission on Social Determinants of Health (CSDH). Closing the gap in a generation: Health equity through action on the social determinants of health. Final Report of the Commission on Social Determinants of Health. Geneva: WHO; 2008.
31. Hunt SA, Abraham WT, Chin MH, Feldman AM, Francis GS, Ganiats TG, et al. ACC/AHA 2005 Guideline update for the diagnosis and management of chronic heart failure in the adult: A report of the American College of Cardiology/American Heart Association Task Force on practice guidelines (Writing committee to update the 2001 guidelines for the evaluation and management of heart failure): Developed in collaboration with the American College of Chest Physicians and the International Society for Heart and Lung Transplantation: Endorsed by the Heart Rhythm Society. Circulation. 2005; 112:e154–e235. [PubMed: 16160202]
32. Bibbins-Domingo K, Chertow GM, Coxson PG, Moran A, Lightwood JM, Pletcher MJ, et al. Projected effect of dietary salt reductions on future cardiovascular disease. N Engl J Med. 2010; 362:590–9. [PubMed: 20089957]
33. Reddy, KS.; Gupta, PC. Tobacco Free Initiative. Report on tobacco control in India. New Delhi: Ministry of Health and Family Welfare, Government of India; 2008.
34. Gupta, PC.; Asma, S., editors. Bidi smoking and public health. New Delhi: Ministry of Health and. Family Welfare, Government of India; 2008.
35. Chaloupka, FJ.; Hu, TW.; Warner, KE.; Jacobs, R.; Yurekli, A. The taxation of tobacco products. In: Jha, P.; Chaloupka, F., editors. Tobacco control in developing countries. Oxford: Oxford University Press; 2000. p. 877-83.
36. Gaziano TA, Galea G, Reddy KS. Scaling up interventions for chronic disease prevention: The evidence. Lancet. 2007; 370:1939–46. [PubMed: 18063028]
37. Oxman AD, Bjørndal A, Becerra-Posada F, Gibson M, Block MA, Haines A, et al. A framework for mandatory impact evaluation to ensure well informed public policy decisions. Lancet. 2010; 375:427–31. [PubMed: 20113827]
38. Dahlöf B, Lindholm LH, Hansson L, Scherstén B, Ekbom T, Wester PO. Morbidity and mortality in the Swedish trial in old patients with hypertension (STOP-Hypertension). Lancet. 1991; 338:1281–5. [PubMed: 1682683]

39. Kostis JB, Davis BR, Cutler J, Grimm RH Jr, Berge KG, Cohen JD, et al. Prevention of heart failure by antihypertensive drug treatment in older persons with isolated systolic hypertension: SHEP Cooperative Research Group. JAMA. 1997; 278:212–16. [PubMed: 9218667]
40. Staessen JA, Fagard R, Thijs L, Celis H, Arabidze GG, Birkenhäger WH, et al. Randomised double-blind comparison of placebo and active treatment for older patients with isolated systolic hypertension. The Systolic Hypertension in Europe (Syst-Eur) Trial Investigators. Lancet. 1997; 350:757–64. [PubMed: 9297994]
41. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, et al. National Heart, Lung, and Blood Institute Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; National High Blood Pressure Education Program Coordinating Committee. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: The JNC 7 report. JAMA. 2003; 289:2560–72. [PubMed: 12748199]
42. Hunt SA, Abraham WT, Chin MH, Feldman AM, Francis GS, Ganiats TG, et al. 2009 focused update incorporated into the ACC/AHA 2005 Guidelines for the Diagnosis and Management of Heart Failure in Adults: A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines: Developed in collaboration with the International Society for Heart and Lung Transplantation. Circulation. 2009; 119:e391–e479. [PubMed: 19324966]
43. Williams B, Poulter NR, Brown MJ, Davis M, McInnes GT, Potter JF, et al. BHS guidelines working party, for the British Hypertension Society. British Hypertension Society guidelines for hypertension management 2004 (BHS-IV): Summary. BMJ. 2004; 328:634–40. [PubMed: 15016698]
44. Kjekshus J, Pedersen TR, Olsson AG, Faergeman O, Pyörälä K. The effects of simvastatin on the incidence of heart failure in patients with coronary heart disease. J Card Fail. 1997; 3:249–54. [PubMed: 9547437]
45. Lewis SJ, Moye LA, Sacks FM, Johnstone DE, Timmis G, Mitchell J, et al. Effect of pravastatin on cardiovascular events in older patients with myocardial infarction and cholesterol levels in the average range: Results of the Cholesterol and Recurrent Events (CARE) trial. Ann Intern Med. 1998; 129:681–9. [PubMed: 9841599]
46. Prevention of cardiovascular events and death with pravastatin in patients with coronary heart disease and a broad range of initial cholesterol levels. The Long-Term Intervention with Pravastatin in Ischaemic Disease (LIPID) study group. N Engl J Med. 1998; 339:1349–57. [PubMed: 9841303]
47. Effect of enalapril on mortality and the development of heart failure in asymptomatic patients with reduced left ventricular ejection fractions. The SOLVD Investigators. N Engl J Med. 1992; 327:685–91. [PubMed: 1463530]
48. Flather MD, Yusuf S, Køber L, Pfeffer M, Hall A, Murray G, et al. Long-term ACE-inhibitor therapy in patients with heart failure or left-ventricular dysfunction: A systematic overview of data from individual patients. ACE-Inhibitor Myocardial Infarction Collaborative Group. Lancet. 2000; 355:1575–81. [PubMed: 10821360]
49. Dargie HJ. Effect of carvedilol on outcome after myocardial infarction in patients with left-ventricular dysfunction: The CAPRICORN randomised trial. Lancet. 2001; 357:1385–90. [PubMed: 11356434]
50. Antman EM. Glycoprotein IIb/IIIa inhibitors in patients with unstable angina/non-ST-segment elevation myocardial infarction: Appropriate interpretation of the guidelines. Am Heart J. 2003; 146(4 Suppl):S18–S22. [PubMed: 14564302]
51. Effects of ramipril on cardiovascular and microvascular outcomes in people with diabetes mellitus: Results of the HOPE study and MICRO-HOPE substudy. Heart Outcomes Prevention Evaluation Study Investigators. Lancet. 2000; 355:253–9. [PubMed: 10675071]
52. Lindholm LH, Dahlöf B, Edelman JM, Ibsen H, Borch-Johnsen K, Olsen MH. LIFE study group. Effect of losartan on sudden cardiac death in people with diabetes: Data from the LIFE study. Lancet. 2003; 362:619–20. [PubMed: 12944063]

53. Patel A, MacMahon S, Chalmers J, Neal B, Billot L, Woodward M, et al. Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes. ADVANCE Collaborative Group. N Engl J Med. 2008; 358:2560–72. [PubMed: 18539916]
54. Gerstein HC, Miller ME, Byington RP, Goff DC Jr, Bigger JT, Buse JB, et al. Action to Control Cardiovascular Risk in Diabetes Study Group. Effects of intensive glucose lowering in type 2 diabetes. N Engl J Med. 2008; 358:2545–59. [PubMed: 18539917]
55. Karthikeyan G, Mayosi BM. Is primary prevention of rheumatic fever the missing link in the control of rheumatic heart disease in Africa? Circulation. 2009; 120:709–13. [PubMed: 19667233]
56. Rheumatic fever and rheumatic heart disease: Report of a WHO Expert Consultation, Geneva 29 October–1 November 2001. World Health Organ Tech Rep Ser. 2004; 923:1–122. [PubMed: 15382606]
57. Nordet P, Lopez R, Dueñas A, Sarmiento L. Prevention and control of rheumatic fever and rheumatic heart disease: The Cuban experience (1986–1996–2002). Cardiovasc J Afr. 2008; 19:135–40. [PubMed: 18568172]
58. Arguedas A, Mohs E. Prevention of rheumatic fever in Costa Rica. J Pediatr. 1992; 121:569–72. [PubMed: 1403390]
59. Soudarssanane MB, Karthigeyan M, Mahalakshmy T, Sahai A, Srinivasan S, Subba Rao KS, et al. Rheumatic fever and rheumatic heart disease: Primary prevention is the cost effective option. Indian J Pediatr. 2007; 74:567–70. [PubMed: 17595500]
60. Ntsekhe M, Wiysonge C, Volmink JA, Commerford PJ, Mayosi BM. Adjuvant corticosteroids for tuberculous pericarditis: Promising, but not proven. QJM. 2003; 96:593–9. [PubMed: 12897345]
61. Investigation of the Management of Pericarditis in Africa (IMPI Africa). [23 August 2010] ClinicalTrials.gov identifier: NCT00810849. Available at http://clinicaltrials.gov/ct2/show/NCT00810849
62. Brilakis ES, Hernandez AF, Dai D, Peterson ED, Banerjee S, Fonarow GC, et al. Quality of care for acute coronary syndrome patients with known atherosclerotic disease: Results from the Get With the Guidelines Program. Circulation. 2009; 120:560–7. [PubMed: 19652090]
63. Fonarow GC, Abraham WT, Albert NM, Gattis Stough W, Gheorghiade M, Greenberg BH, et al. Influence of a performance-improvement initiative on quality of care for patients hospitalized with heart failure: Results of the Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients With Heart Failure (OPTIMIZE-HF). Arch Intern Med. 2007; 167:1493–502. [PubMed: 17646603]
64. Fonarow GC, Albert NM, Curtis AB, Stough WG, Gheorghiade M, Heywood JT, et al. Improving evidence-based care for heart failure in outpatient cardiology practices: Primary results of the Registry to Improve the Use of Evidence-Based Heart Failure Therapies in the Outpatient Setting (IMPROVE HF). Circulation. 2010; 122:585–96. [PubMed: 20660805]
65. Abegunde DO, Shengelia B, Luyten A, Cameron A, Celletti F, Nishtar S, et al. Can non-physician health-care workers assess and manage cardiovascular risk in primary care? Bull World Health Organ. 2007; 85:432–40. [PubMed: 17639240]

Table I

The cardiovascular disease health transition that results from population and epidemiological transitions in many societies

Health transition: Cardiovascular disease example				
Stage	**I**	**II**	**III**	**IV**
Life expectancy (years)	35	50	60	>70
Dominant diseases	Infections, nutritional	Mixed (receding communicable and rising non-communicable)	Chronic (mid-life)	Chronic (elderly)
Contribution of cardiovascular disease to mortality (%)	5–10	15–35	>50	<50
Pattern of cardiovascular disease	Rheumatic, nutritional	Rheumatic, nutritional and stroke (ICH)	Coronary, stroke (both)	Coronary, stroke (THR)
Primary victims	Higher class	All classes	Lower classes	Lower classes

Model developed by Omran; modified by Olshansky and Ault ICH intracranial haemorrhage THR thrombotic