



Heartfile

PREVENTING CORONARY HEART DISEASE In South Asia



SAARC Cardiac Society Guidelines and Recommendations

Sania Nishtar



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The South Asian Association for Regional Cooperation (SAARC) was established in 1985 at the First SAARC Summit held in Dhaka, Bangladesh, even though [ideas](#) for regional grouping of South Asian nations had been mooted since 1980. Currently made up of Bangladesh, Bhutan, India, Maldives, Nepal, Pakistan and Sri Lanka, SAARC's main goal is to accelerate economic and social development in member states through joint action in certain agreed areas of cooperation. The SAARC Cardiac Society is an official affiliate of the SAARC framework with the overall objective of fostering cooperation between member countries in the area of cardiovascular disease control. The development of these clinical guidelines and recommendations is part of this initiative.

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PREFACE

South Asia, housing more than half of the world's poor and illiterate and constituting 23% of the world's population is a notable reality in the face of the cardiovascular disease epidemic. The meager per capita average budgetary expenditure on health ranging between US \$ 11-20¹ for different countries of the region further highlights this challenge. The prevention and control of cardiovascular diseases is therefore one of the major health care issues faced by South Asia; the fact that this remains largely unrecognized adds to the gravity of the situation. Cardiovascular diseases are low on the list of priorities in these countries where reproductive and communicable disease issues dominate health care; the economic impact of these diseases and its implications for disadvantaged groups also remains largely unrecognized. A significant lack of awareness about the magnitude of the problem at all levels and a consequent lack of will to address this issue is therefore likely to have serious implications.

In order to address this issue effectively in the South Asian context several simultaneous approaches at the policy and program level need to be set into action as a priority. Major challenges at the policy level are anticipated, but counters to those exist; several opportunities also exist at the program level, which have the potential to integrate the preventive approach to cardiovascular diseases with the current health agendas in these countries in a time and cost efficient manner; an attempt has been made to identify these. In addition, several considerations unique to the South Asian setting need to be recognized and addressed at the professional level in a public health and clinical framework.

These considerations call for the formulation of recommendations and guidelines at all levels for the prevention of cardiovascular diseases in the region. The need to formulate these guidelines and recommendations is made even more urgent as disease prevention and health promotion are the

only affordable solutions for the vast populations of South Asia. Classical medical interventions are, and will continue to remain, inaccessible to the majority of the population in the short to medium term. The compelling driving force behind this approach is the understanding that South Asia cannot afford a full-blown CVD epidemic. We therefore must do all that we can to prevent it.

This document presents recommendations and clinical guidelines for the prevention and management of coronary heart disease, which is the principal preventable cardiovascular disease. However it must be recognized that all major preventable cardiovascular diseases and indeed many other non-communicable diseases are linked by common preventable risk factors and can be addressed through a common preventive strategy.

I am very grateful to all the members of the SAARC and the Regional Consensus Panels for their valuable input and members of the International Advisory Board for their guidance. I also wish to take this opportunity to thank especially, members of my team at Heartfile: Dr. Saulat Yar Khan, Yasir Abbas Mirza, Dr. Yasmin Hadi and Dr. Asma Badar for all the support that they lent me for this task and lastly my especial thanks to Prof. Upendra Kaul, Secretary General of the SAARC Cardiac Society for his help and encouragement all through the preparation of these guidelines.

Islamabad, Pakistan
January 26, 2002

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CORONARY HEART DISEASE PREVENTION GUIDELINES AND RECOMMENDATIONS FOR THE SAARC REGION

Guidelines are systematically developed statements traditionally used to reinforce best practices.ⁱⁱ The principal benefit of guidelines is to improve the quality of care received by patients. Guidelines can also be seen as a way to support effective clinical practice adaptable in individual circumstances and additionally serve as educational tools.ⁱⁱⁱ

The broad interest in clinical guidelines has its origin in issues that health care systems face the world over. These include rising health care costs fueled by increased demand for care, more expensive technologies and an ageing population; variations in service delivery among providers, hospitals and geographic regions; the presumption that at least some of the variation stems from inappropriate care, either overuse or under use of services and the intrinsic desire of healthcare professionals to offer, and of patients to receive, the best care possible.^{iv} In South Asia, developing clinical guidelines to optimize health care delivery is a major challenge as the level of care varies dramatically from place to place. The thickly populated urban areas are technologically advanced while the rural areas often fall short of the bare minimum of health care provision.

Several guidelines within the framework of primary and secondary prevention of coronary heart disease (CHD) have been developed as part of an effort to standardize practice in the developed world, drawing recommendations based on outcome data from randomized clinical trials;^v some of these guidelines have also graded recommendations based on the levels of evidence.^{vi} Such guidelines have been guiding clinical practice in the region but are unable to address issues relating to cost of care and unavailability of options. Therefore, their impact on clinical practice is limited. It is with this perspective and needs assessment that guidelines for preventing CHD in the South Asia have been developed. Guidelines for South Asia can be appropriately targeted to a population belonging to the

same ethnic group, sharing cultural similarities, geographic proximity, economic priorities, and similar epidemiological characteristics of cardiovascular disease.^{vii} This need was emphasized upon at the executive council meeting of the SAARC Cardiac Society in July 2000, where it was proposed that a series of practice guidelines be formulated for the region through consensus amongst member countries. The first in this series are guidelines for the prevention of CHD in South Asia.

In addition to clinical guidelines, this documents also addresses key public health and policy issues specific to South Asia and summarizes public health and policy recommendations that have been identified as being crucial to the preventive approach to CHD in the region. Prevention of CHD has been categorized under primordial, primary and secondary, employing both behavioral and drug interventions with recommended goals. Tertiary prevention has not been dealt with. Recommendations highlight the public health and clinical approaches, with considerable overlap. Key policy issues relating to heart disease prevention have been alluded to in an attempt to sensitize clinicians to the crucial relevance of policy changes in the larger perspective of *Cardiovascular disease prevention*.

THE GLOBAL BURDEN OF CARDIOVASCULAR DISEASE

Cardiovascular disease has probably been the world's leading cause of death for at least the last two decades of the 20th century.^{viii} In the year 1999, 16,970,000 people died due to cardiovascular diseases worldwide, which accounts for 30.3% of all the deaths worldwide.^{ix} Cardiovascular diseases additionally account for more than 10% of DALYs¹ in middle to lower income countries and 18% of DALYs in high-income countries. Within CVD, which account for about one in eight DALYs globally, ischaemic heart disease and cerebrovascular disease are the most significant.^x In future, cardiovascular diseases are expected to become even more common with the aging of the world population.^{xi}

It has been estimated that non-communicable disease mortality will increase from 28.1 million deaths in 1990 to 49.7 million in 2020.^{xii} The top three contributors to the burden of disease in 2020 are predicted to be ischaemic heart disease, followed by unipolar depression and road-traffic accidents. This disease trend has been extrapolated from existing data based on what has been termed the *Epidemiological Transition*. This term was coined to describe the shift in the disease spectrum from communicable to non-communicable diseases. Previously communicable diseases and reproductive health issues were the overwhelming health concerns worldwide, alongside nutritional deficiencies. Then as the industrialized world became developed these diseases were more or less brought under control and non-communicable diseases such as cancer, heart disease and stroke became a significant concern. Indeed, cardiovascular diseases make up the greater part of the non-communicable diseases. These diseases came in the wake of major demographic and lifestyle changes such as falling infant mortality, rising life expectancy, urbanization and increasing

¹ DALY is a way of measuring health status by quantifying not merely the number of deaths but the impact of premature death and disability on populations and combines them into the Disability-Adjusted Life Year or DALY.

gross national product and per capita income that were taking place in the developed world at the time, and have resulted in increased food consumption, tobacco usage and decreased physical activity.

This transition has already occurred in the developed world. The economies in transition are in the throes of the epidemiological transition and now it is the turn of the developing world. It is not widely realized that at present the developing countries contribute a greater share to the global burden of CVD than the developed countries and nothing less than an explosion in disease burden is projected over the coming years^{xiii} termed as the impending global pandemic of cardiovascular diseases.^{xiv}



PROFILE OF SOUTH ASIA

According to World Bank, a dollar a day estimates, out of the 1.3 billion people in the world who live below the poverty line, 515 million (40%) live in South Asia even though the region accounts for only 23% of the global population.^{xv} South Asia is one of the poorest, the most illiterate, the most malnourished, the least gender-sensitive, indeed, one of the most deprived regions in the world. This gap is also evident by comparing the South Asian GNP per capita (US \$) of 437 to 1240 for the rest of the developing world.^{xvi}

According to the Human Development Report in South Asia 1999,^{xvii} the total estimated population of this region in 1998 was 1313 million people. With the total estimated population of the world at 6 billion, it can be seen that a sizable portion of humanity lives in the SAARC region. The annual population growth rate of South Asia is about 2% compared with 1.8% for the rest of the developing world. For this vast mass of mankind, the average public sector expenditure on health (as a percentage of the GDP) was 0.85 in 1997 compared to 2.0% for the rest of the developing world. Additionally for every dollar of central government expenditure spent on social sectors, \$8.65 is spent on defense and debt servicing in Pakistan, and \$3.12 in India, further highlighting the economic and political considerations that constrain the health care scenario in the region.^{xviii}

Cost is therefore a major issue in sustainability and compliance with any treatment, and is one of the major factors determining disease outcomes in the SAARC region.

Monthly household incomes in the rural and the urban areas of various South Asian countries and the percentages of the health expenditure borne by the private and the public sector have been tabulated (Table 1). All these figures highlight the constraints of the private and the public sector to invest in cardiovascular health care. This is further highlighted through a

Table 1² Average monthly household income and per-capita health expenditure in South Asian countries (US \$)

	Pakistan	India	Bangladesh	Nepal	Sri Lanka
Rural income	81,75	45,06	63,45	50,73	66,52
Urban income	110,13	53,32	138,30	74,77	133,04
Household size	6,70	5,60	5,00	5,10	5,50
Per person income (rural)	12,20	8,05	12,68	9,95	12,08
Per person income (urban)	16,43	9,52	27,65	14,66	24,18
Total per-capita health expenditure	18	20	12	11	26
% health expense (private sector)	77,5	84	52,78	76,36	54,84
Private sector per-capita health expense	13,95	16,8	6,33	8,4	14,26
% health expense (public sector)	22,5	16	47,22	23,64	45,16
Public sector per-capita health expense	4,05	3,2	5,67	2,6	11,74

comparison of the monthly expenditure on various therapeutic packages for the management of high blood pressure and lipid lowering with the annual rural and urban household incomes and when viewed as a percentage of the average household health expenditure by the private and the public sector (Appendix A).

With South Asia now on the verge of a cardiovascular explosion, its inability to invest meaningfully in therapeutic cardiovascular care is apparent. South Asia cannot afford to treat cardiovascular disease; therefore in addition to an emphasis on prevention, cost-effective clinical and public health approaches to the issue must evolve through consensus; these approaches should be based not only on evidence but also on the reality of what is feasible.

² Monthly household incomes and household sizes have been quoted from the Economic Reviews of the respective countries. Average monthly household incomes have been converted into US dollars based on the exchange rates as of July 18, 2001 displayed on <http://theFinancial.com>. Per capita health expenditure has been quoted from the World Bank Report: 2001, World Development Indicators, The World Bank, Washington 2001. Health expenditure and the percentages of the total health expenditure borne by the private and the public sector have been calculated from figures given in the same report.



EPIDEMIOLOGY OF CORONARY HEART DISEASE

South Asian Immigrant Population

An insight into the South Asian coronary risk comes from the study of the prevalence rates (mortality and morbidity data) amongst the expatriate South Asian population, which reveal that South Asians, as an ethnic entity have increased prevalence and definite evidence of excess mortality from CHD as compared to any other ethnic group.^{xviii,xix} This phenomenon was described initially for the colonial plantation workers in the Pacific islands in the early 1950's,^{xx} and was later confirmed by mortality and morbidity data from UK and USA,^{xxi,xxii} and subsequently from other parts of the world.^{xxiii,xxiv,xxv,xxvi,xxvii} Similarly, recent data from Canada shows that being of South Asian ethnic origin carries 4.51 higher odds of CHD as compared to Europeans after adjusting for both conventional as well as novel risk factors.^{xxviii}

In addition to high prevalence, CHD is known to have a significantly younger onset and is known to be more aggressive in its presentation.^{xxix} This excess CHD risk cannot be explained entirely in each South Asian sub group by conventional risk factors alone.^{xix,xxx} Data reveals that expatriate South Asians do however suffer from an increased risk of non-insulin dependent diabetes mellitus (NIDDM),^{xxxi} together with adverse fat distribution, hyperinsulinemia and insulin resistance relative to other ethnic groups.^{xxxii} This, known as the Insulin Resistance Syndrome is known to underlie the increased coronary risk in South Asian populations.^{xxxiii} Alterations in body fat distribution particularly increased visceral fat may contribute to these abnormalities.^{xxxiv,xxxv} Insulin resistance has also been associated with inflammation,^{xxxvi} C-reactive protein (CRP), which is a sensitive marker of systemic inflammation, has been shown to be higher in healthy Asian Indians than in European whites^{xxxvii} and has been accounted for by greater central obesity and insulin resistance. This also highlights a possible

mechanism for the increased coronary risk in this population. South Asians are also known to have higher levels of triglycerides, lower HDL cholesterol (HDL) and relatively normal cholesterol levels as compared to Caucasians.^{xix,xxxviii,xxxix} These may mediate atherogenic changes in the presence of relatively lower LDL cholesterol (LDL) levels reported for this population and raise the question of LDL lowering by amount or the utilization of triglycerides and HDL as primary goals for this population. Insulin resistance also increases small dense LDL particles, which may also contribute to the increased lipid related coronary risk in this population.^{xi} Further research is needed to clarify these issues.

For the expatriate population, the effect of migration on coronary risk is also important. Between countries comparisons (UK and India) have shown that migration confers a higher risk of CHD with an increase in body weight, serum cholesterol, and blood pressure. There is additionally a trend towards the acquisition of westernized behaviors consistent with a sedentary lifestyle, high salt and fat and low fiber diet and new stresses. The likelihood of increase in insulin resistance, its expression as frank diabetes mellitus and glucose intolerance probably increases on migration. A combination of these factors may therefore unmask the underlying genetic risk of CHD.^{xli}

The role of novel risk factors for CHD is now emerging; South Asians have also been reported to have higher homocysteine levels^{xlii} and elevated PAI-1 and fibrinogen levels as compared to native white populations;^{xxviii,xliii} but there are, as yet, no clear answers to ascribe the increased coronary risk to a distinct risk profile. The risk factor profile of this population may also be continuously evolving as both the emigrant as well as the indigenous South Asian populations are undergoing rapid urbanization and acculturation of western lifestyles and behaviours, acting upon an, as yet unidentified susceptible genotype.

South Asian Indigenous Population

For preventive strategies the definition of the risk factor profile of a population to set targets for intervention and goals for preventative initiatives is crucial. For the South Asian population this has been complicated by several factors. Lessons learned from the expatriate coronary risk highlight increased mortality and morbidity trends that are partially unaccounted for by the traditional risk factor profile; the prevalence of traditional risk factors

has not been well documented within the native populations; causal and temporal relationships between the risk factors have not been established and against the backdrop of these current gaps in our knowledge, insufficient work has been done on the role of novel risk factors.

The public health response to this issue on one hand, must include health research that serves to inform policy and the subsequent initiation of preventive programmes. On the other hand, it demands, in synergism with the requirements for a concerted cost-effective clinical approach to this issue, a set of guidelines based on the currently existing level of knowledge. It may be true that the overall high CHD risk cannot be explained on the basis of these alone, but conventional risk factors for CHD such as smoking, high blood pressure, dyslipidaemia and diabetes are strongly associated with CHD in South Asians^{xliv} and will remain the key if not the only elements of the risk factor model in this population. It is therefore prudent to set goals and targets for preventive initiatives based on the traditional risk factor profile; within this paradigm it is essential to emphasize targeting the risk characteristics that have been demonstrated as the key elements of the South Asian risk profile.

Several biological, behavioural, psychological and social risk factors have been recognized as risk factors for CHD; several aspects need to be recognized in this context. Firstly, the risk for most biological variables operates on a continuum of progressive increase over a wide range, rather than across abrupt arbitrary thresholds, which spells out the need to address the risk factor distribution in a population rather than deal only with those at the extreme high end. Secondly multiplicative risk arising from a combination of risk factors has also been recognized from several large longitudinal studies; it is now clear that the largest proportion of CVD events in any community arises from persons who have modest elevations of many risk factors than from individuals with marked elevation of a single risk factor. And thirdly clustering of CVD risk factors is also common due to similar life-style associations, which provides an opportunity to adopt integrated strategies of multi-factorial risk reduction.^{xiv} There is therefore the need to address “risk profiles” rather than “a risk factor” with a potential for therapeutic intervention across a certain threshold.^{xiv} The available sketchy data on the epidemiology of CHD in indigenous South Asians and its risk states is discussed.

Coronary heart disease: prevalence of CHD has been reported from India at 4% in the rural^{xlvi} and 11%^{xlvii} in the urban population whereas in Pakistan 7% of the population over the age of 65 years have reported to have been hospitalized for a myocardial infarction.^{xlviii}

Hypertension: the positive relationship between systolic and diastolic blood pressure and cardiovascular disease has long been recognized. In India, the prevalence of hypertension defined by JNC-V1 criteria has shown a steep increase from 6.2% in 1959^{xlix} to 30.9% in 1995.¹ According to the National Health Survey of Pakistan,ⁱⁱ hypertension (defined as a systolic blood pressure of over 140 and diastolic over 90 mm hg) affects 17.9% of adults 15 years of age and over and 33% of adults 45 years of age and over. Overall urban Pakistanis have higher prevalence of high blood pressure than rural dwellers (21.5% vs. 16.2%). The unawareness rate in this survey has been reported at 70%, which is amongst the highest in the world. Hypertension (defined as a diastolic blood pressure over 90) has a prevalence rate of 12.7% amongst females and 20% amongst males in Sri Lanka,ⁱⁱⁱ while in Bangladesh a prevalence of 11.3%ⁱⁱⁱⁱ has been reported. In Bangladesh, the Household Expenditure Survey of 1995-1996 showed an average daily intake of 15 grams of salt,^{lv} which is far above the recommended levels and has significant implications for health promotion.

Smoking: smoking is the principal preventable risk factor for cardiovascular diseases and is now beginning to be recognized as a risk factor for atherothrombotic events.^{lv} Tobacco-use is highly prevalent in South Asia; tobacco is smoked in several forms such as in the hukka,³ beeri⁴ and cigarettes in addition to the practice of chewing tobacco in the form of "pan".⁵ In both the urban and rural populations in India, tobacco use is widely prevalent. Studies have shown that 39% urban and 51% rural men in Rajasthan (India) either smoke or consume tobacco in some form.^{lvi} In Pakistan 34% men and 12.5% women use some form of tobacco on a regular basis.^{lvii} The prevalence of smoking in Sri Lanka has also reported to be high, ranging between 53-58% in the 35-59 years age group^{lviii} while in Bangladesh 57% men and 23.2% women over the age of 18 years use tobacco.^{lviii} The prevalence of smokeless chewable tobacco is very high in South Asia with over 10% of the population in Pakistan, 22% of men in India

³ Device for smoking tobacco which is alike the middle eastern "hubble bubble"; tobacco is heated in a pot and is made to pass through water cisterns before being inhaled though a long tube; the device is used for communal smoking.

⁴ Beeri is a local form of cigarette in which tobacco is rolled in a leaf.

⁵ Betel leaf eaten with condiments, which may include tobacco.

and 16% men and 21% women in Bangladesh^{lviii} using chewable tobacco. The cardiovascular effects of chewable tobacco are similar to those of cigarette smoking.^{lix} However the age adjusted relative risk of dying from CVD is lower with smokeless tobacco than with tobacco smoking.^{lx}

Diabetes: diabetes mellitus is a major risk factor for CVD and is designated a CHD risk equivalent in Adult Treatment Panel III^{lxi} (ATP III); compared with their non-diabetic counterparts, the relative risk for CHD for men with diabetes is two to three and that for women with diabetes is three to four.^{lxii, lxiii, lxiv} According to The National Health Survey of Pakistan,^{li} defining diabetes as a random blood sugar of 140 mg% and over, there are 2.7 million people in Pakistan who may have diabetes, yet only 0.8% are diagnosed; prevalence being highest amongst obese urban dwellers. Urban females aged 45-64 years have the highest prevalence of diabetes at 18%, whereas rural females of the same age have a prevalence of 7%. Males aged 45-64 years have a prevalence of 9% in the urban and 5% in the rural areas. In India, the prevalence of diabetes has been variably reported at 1.3% to 2.4% in the rural and 3.0 to 8.4% in the urban areas.^{lxv, lxvi} In Sri Lanka, the prevalence is reported at 4.8% in males.^{lxvii} Studies in Bangladesh have shown that the age-standardized prevalence of impaired glucose tolerance is 7.7% whereas the prevalence of NIDDM has been reported at 4.5%.^{lxviii}

The Metabolic syndrome: the metabolic syndrome represents a constellation of lipid and non-lipid related risk factors of metabolic origin, recently a genetic basis for this has been hypothesized^{lxix} and chronic sub-clinical inflammation has been reported as being part of this syndrome.^{xxxvi} This syndrome is linked to the generalized metabolic disorder called insulin resistance in which the normal actions of insulin are impaired. Increased body fat (particularly abdominal obesity) and physical inactivity promote the development of insulin resistance.

Asian Indians are known to be more prone to central obesity, insulin resistance and glucose intolerance relative to other ethnic groups.^{lxx, lxxi} Abdominal obesity, a pattern of obesity as measured by waist circumference has emerged as an even more important risk factor for CHD than total body adiposity, and is more closely associated with cardiovascular disease risk factors studied than overall adiposity as measured by BMI.^{lxxii, lxxiii} A very high prevalence of waist hip ratio among men (0.95) and women (0.85) and

truncal obesity in both urban (men 39.1%, women 70.9%) as well as rural subjects (men 32.4%, women 42.3%) was reported from Delhi, India.^{lxxiv} Recent studies have identified that the simultaneous measurements and interpretation of simple variables, such as waist circumference and fasting plasma triglycerides concentrations, could be used as inexpensive screening tools for the identification of men characterized by the atherogenic metabolic triad;^{lxxv} this may be particularly relevant in the South Asian context.

Generalized obesity and lack of physical activity: obese adults experience higher rates of CVD.^{lxxvi} Obesity is often present in association with the other risk factors for CHD and this grouping further increases the risk. In Sri Lanka, 18.2% of the population was found to be obese (defined as BMI>24), whereas 20.9% of the population was labeled as leading a sedentary life.^{lxxvii} A 10% prevalence rate of obesity amongst rural males and 20% amongst urban females has been reported from Pakistan.^{li}

Individuals who engage in regular physical activity have lower prevalence rates of cardiovascular risk factors; exercise has also been found to yield beneficial effects on several risk factors and is therefore considered an important adjuvant therapy in risk factor modification.^{lxxviii} For the South Asian population this offers a cost-effective opportunity for risk reduction.

Diet: it may seem that dietary practices vary in South Asia; diet in the North West Frontier province of Pakistan is rich in animal fat and red meat; in Sri Lanka food is predominantly cooked in coconut oil; in Bangladesh fish is the staple diet whereas in parts of India vegetarianism is the norm. The common element in these seemingly diverse dietary habits is the style of cooking, which is curry based and consumes a large quantity of fat. Additionally, with the trend of urbanization and acculturation of westernized lifestyles, there is an added concern relating to a diet even higher in salt, saturated fat and refined carbohydrates. Dietary modification for this population offers a great opportunity for risk factor intervention particularly since this can be packaged as a cost-effective approach. This is further reinforced by provocative evidence suggesting that a diet emphasizing more bread, more root and green vegetables, more fish, less beef and lamb replaced with poultry, no day without fruit, and substitution of butter and cream has effects that may be superior to those observed for the American Heart Association Step I diet.^{lxxix}

Dyslipidaemia: results of some studies from India have been consistent with a greater role for total and LDL cholesterol in mediating coronary risk^{xlvii} while results of others have revealed that coronary artery disease occurs in Indians at low lipid levels.^{xxxix} Recent unpublished data from the RISKORN⁶ study in Pakistan also indicates that CHD occurs at relatively normal total cholesterol and LDL levels and indicates that CHD in this population is HDL rather than LDL driven. The evidence for the association between low HDL and CHD is quite strong; much of it derived from prospective epidemiological studies.^{lxxx,lxxxi,lxxxii} Recent meta-analysis of prospective studies show that elevated triglycerides are also an important independent risk factor of CVD whereas low HDL-cholesterol both modifies the goal for LDL lowering therapy and is used as a risk factor to estimate the 10-year risk for CAD in the ATP III guidelines.

Studies have also indicated that Lipoprotein(a) levels are elevated in people of South Asia origin;^{xli,lxxxiii,lxxxiv} however this needs to be interpreted with caution as the mechanisms by which Lp(a) is associated with CHD are not entirely clear; this is further complicated by lack of consensus on laboratory measurements of Lp(a). The atherogenicity of Lp(a) is reduced in association with reductions in LDL cholesterol levels. Indians are known to acquire higher LDL cholesterol concentrations compared to the native white population on migration, with a trend towards the acquisition of westernized behaviours; therefore the increases in serum cholesterol after migration may unmask the underlying genetic risk of CAD conferred by high serum Lpa.^{xli}

In India, the prevalence of hypercholesterolaemia (defined as >200 mg/dl), in the industrial, urban and rural populations in Delhi was reported at 30.9%, 36.8% and 16.3% respectively in men, and 21.7%, 39.7% and 16.3% in women. There were however, significant numbers with low HDL cholesterol, (<40 mg/dl) and high triglycerides (>150 mg/dl).^{lxxxiv} Serum cholesterol levels are reported to be over 6.5 mmol/l in 7.6% of rural and 14.9% of urban Sri Lankan population, and range between 5.2- 6.5 mmol/l in 27.9% of rural and 26.5% of the urban population respectively.^{lxxxv} In Pakistan, 12.6% of the population over 15 years of age is reported to have serum cholesterol level over 200 mg/dl.⁵¹

⁶ A case-control study of the risk factors for coronary artery disease in a Pakistani population. Pakistan Institute of Medical Sciences, Islamabad, Pakistan and St Thomas hospital London, UK. Supported by the Pakistan Medical Research Council.

Stress: recent studies provide clear and convincing evidence that psychosocial factors contribute significantly to the pathogenesis and expression of CHD; this evidence is composed largely of data relating CHD risk to depression,^{lxxxvi} anxiety, personality factors and character traits such as anger,^{lxxxvii} social isolation, and chronic life stress.^{lxxxviii} Emotionally stressed younger patients are also known to represent high-risk groups.^{lxxxix}

Expatriate South Asians have additional stresses in the host country related to social class, cultural isolation and racism in addition to the known risk factors for CHD operating in the host country; studies carried out on civil servants in UK have indicated that South Asians as compared to whites suffer from higher levels of stress; these findings are consistent with ethnic differences in coronary risk.^{xc} Native South Asians, however, may have a whole host of as yet poorly identified and measured psychosocial and economic stress factors.^{xc,xcii} Changes in the South Asian society such as urbanization, break down of family and social support systems, shift from a rural agrarian to a service and manufacturing economy while facing acute demographic and economic pressures are expected to increase both universal and culturally specific CVD stresses in future.^{xciii}

Physical characteristics: low birth weight, thinness and short body length at birth are known to be associated with increased rates of cardiovascular disease and non-insulin dependent diabetes later in life.^{xciv,xcv} Recently low birth weight is reported to be associated with endothelial dysfunction in young adults; an effect most marked in individuals with lower risk factor profiles and may be relevant to the pathogenesis of atherosclerosis in later life.^{xcvi} Data from India supports the high rates of CHD amongst those studied whose mothers had a low body weight during pregnancy. The highest prevalence of disease (20%) was in people who weighed 5.5 lb (2.5 kg) or less at birth and whose mothers weighed less than 100 lb (45 kg) in pregnancy.^{xcvii} The hypothesis needs to be further tested in the South Asian population.

Socioeconomic factors and social support: several studies have confirmed a graded, inverse relation between socioeconomic strata (SES) and the risk of CAD, CVD and all-cause mortality.^{xcviii,xcix,c} There is also an inverse relationship between SES and conventional risk factors.^{ci} Concurrence of risk factors; that can have a synergistic effect on the risk for CVD^{cii} has been shown to be higher in less educated groups.

Childhood poverty followed by high standards of living is known to operate at least partly as a risk factor of coronary heart disease though conventional risk factors.^{ciii} Lower SES in childhood is associated with higher levels of hostility, depression and hopelessness; greater tobacco consumption and alcohol abuse; less leisure time physical activity; obesity and a less nutritious diet in adulthood.^{civ} Socioeconomic factors may be considered as important elements of the risk profile of this population in view of prevailing economic situation; there is potential to further explore this risk factor in the native South Asian setting.

Homocysteine: most of the data on homocysteine is representative of the developed world population, from which the diet of south Asians is known to differ appreciably. In Indian Asians as in other populations of Europe and North America moderately raised levels of plasma homocysteine are associated with an increase in the risk of coronary heart disease; plasma concentrations of homocysteine have been found to be raised in South Asians in comparison to the white population.^{xlii,cv} This difference could be explained on the basis of the lower vitamin B12 and folate levels in Asians. Reduced intake of vitamin B12 has been reported in Asian Indian women;^{cvi} the prolonged cooking of vegetables, which is the common practice in many Asian Indian households, may destroy up to 90% of the folate content.^{cvi} Knowledge of the fact that modification of dietary patterns can have substantial effects on fasting levels of total serum homocysteine opens new doors to evaluate this hypothesis in the South Asian population.^{cviii}

Inflammation: several studies have addressed the possible role of infectious agents in the pathogenesis of atherosclerosis and CHD as a result of which many infectious agents have been implicated in the pathogenesis of CHD. Recently infectious burden has been correlated with CHD^{cix,cx,cxi} and the simultaneous presence of antibodies has been shown to substantially increase the risk for disease development.^{cxii} However, if general infective load is important then the relationship of micro-organisms to CHD in the subcontinent may be more complicated than that seen in temperate climates in the developed world. The hypothesis remains to be tested in the native South Asian population.

C-reactive protein, which is an independent risk factor for CHD has also been shown to be higher in healthy Asian Indians than in European whites

and has been accounted for by greater central obesity and insulin resistance.^{cxiii} Adiposity is also known to be a major determinant of CRP;^{cxiv} this highlights a possible mechanism for the increased coronary risk in this population.

Other risk factors: there are additionally several other risk factors studied in the developed world populations. A discussion of these is outside the scope of this document and is not relevant as there is not only no available data for the indigenous South Asian population on these risk factors, but in addition no significant potential for preventive intervention.

By and large, based on the existing level of knowledge, the South Asian coronary risk appears to be correlated with the insulin resistance/metabolic syndrome; it appears that this syndrome can mediate coronary risk even in the presence of relatively normal total and LDL cholesterol through low HDL cholesterol and high triglycerides. An inflammatory component of this syndrome may mediate part of this risk. Emerging data also supports a genetic basis of the insulin resistance syndrome.^{cxv} It is pure speculation but in future it may be possible to demonstrate a genetic link between the insulin resistance syndrome and Lp(a), both of which are known to play a key role in the mediation of coronary risk in South Asians. Absence of data in these areas highlights serious gaps in our knowledge that need to be bridged in order to understand the increased CHD risk with important implications for prevention. It is therefore imperative to invest in the necessary infrastructure support and local capacity building for research to answer these questions.

THE CONTEXT AND FRAMEWORK OF CHD PREVENTION

Setting the preventive approach of CHD into action in a developing country setting requires the identification of locally relevant issues and existing opportunities for promoting cost and time efficient approaches to CHD prevention. While a preventive population-based approach is commonly acknowledged to be the most cost-effective, paradoxically most of the South Asian countries have adopted a high technology approach to the management of CHD. Technology-intensive management of CHD causes a massive diversion of resources and is unlikely to reduce the toll of CHD in our community. Indeed even the most advanced health systems in the industrial world cannot afford a high technology approach to the CHD epidemic and have turned to prevention-based approaches. Table 2 summarizes details of the cardiovascular resources available as an indication of the present tertiary care base in the region. Even though health systems in these countries have prioritized on tertiary care in CVD, it is evident from the figures that it falls short of the bare minimum. It needs to be additionally recognized that high technology tertiary care of CHD is usually centered on urban areas in South Asia and is accessible to a small minority of the population. This highlights the potential for increasing inequity in health access and outcomes between the haves and have-nots.

The course of the global CHD epidemic over the past 50 years has provided instructive lessons about the best approach to CHD. We know enough about CHD and its determinants that we can work for a future in which heart diseases and stroke could be largely eliminated.^{cxvi} Several biological, behavioural, psychological and social determinants have been recognized as risk factors for CHD. CHD prevention addresses many of these modifiable risk factors, especially lifestyle ones such as smoking, physical inactivity, high blood pressure, dyslipidaemia, obesity, diabetes and psychosocial stress. On the long-term, prevention also contributes to improving the polygenic tendencies which are also strong risk states for

CHD. In populations who do not smoke, are not overweight, maintain a **Table 2⁷** Cardiovascular health services in South Asia

	Pakistan	India	Bangladesh	Nepal	Sri Lanka
Population (million)	141.55	1014	129.19	24.7	19.24
Cardiologists	384	2,500	110	44	14
Cardiac surgeons	19	15,00	25	7	9
Cardiology trainees	12	250	200	4	10
CV nurses	102	N/a	200	67	65
CV technicians	276	N/a	400	28	15
Cardiology departments	18	20	18	4	4
Cardiac surgery units	12	80	2	2	2
Catheter laboratories	13	160	2	1	2
Yearly catheter interventions	532	10,000	100	N/a	N/a
Open heart surgeries	3650	20,000	700	150	N/a

N/a: information not available

healthy diet and exercise moderately or vigorously for half an hour a day and consume alcohol moderately, the incidence of coronary events is more than 50% lower than that in the rest of the population.^{cxvii}

Investment in prevention is highly cost-effective; by controlling CHD risk factors in developed countries, the incidence and mortality rates of CHD have been dropping for years.^{cxviii,cxix} Similar trends have been reported from other developing countries^{cxx} and the same can be expected for the South Asian population. In South Asia, as in several other developing countries,

⁷ Population data (in millions) has been quoted <http://www.geographic.com>, health service data has been taken from the White Book.

there is however, an urgency to prioritize prevention in view of the epidemiological trends of increasing CHD incidence and mortality^{xiii} and the lack of resources to address these public health challenges.

Prevention of CHD before it occurs (primary prevention) needs to be coupled with prevention of complications and proper management once CHD has been established (secondary prevention). It is a priority to promote best practices on both levels of prevention. An important first step is to identify a set of guidelines to reinforce best practices or to encourage such practices by providing “recommendations” that local societies can use to develop guidelines to be used on the country or local level. Several recommendations and guidelines have been developed to guide preventive practices in the developed countries.^{vi,cxxi,cxxii} However such recommendations and guidelines may not be appropriate in the South Asian context. It is therefore imperative to develop culturally-specific and locally-relevant guidelines for the South Asian setting. The following section deals with the issues that are specific to South Asia with regard to CVD prevention and presents the rationale for the recommended approach.

Prevention paradigm

The prevention of cardiovascular diseases is more than a unidirectional initiative even for well developed health systems. The crucial participation of the communities in this effort entailing lifestyle changes; the behavioural, social, political and economic will to forge this change at the level of the individual, the community, the health system and the health policy maker and within that framework the need for health promotion, professional education and advocacy make CVD prevention a multidisciplinary approach involving the health system, industry, communication, trade, commerce, and taxation with implications for the national economy. These considerations have hampered the implementation of the ideal CVD prevention module in the best of circumstances even in the presence of provocative evidence that by investment in *the ideal prevention dose* the incidence of CVD can be dramatically reduced. This is complicated further by a lack of interest in prevention by the commercial and the industrial sector that have a direct interest in promoting curative care.

In developing regions such as in the case of South Asia, these considerations have greater implications in view of the limited resources and

rising CHD trends. This needs to be recognized and warrants an urgent response both at the policy and the programme level to identify effective measures that hold the promise of early impact and to identify opportunities in the South Asian system that are conducive to this approach.

Fostering the political will

Even in the developed countries, there is a sense of complacency of CVD; several health issues of a lesser magnitude generate a far greater public health response as compared to CVD. This can largely be attributed to a lack of awareness at the policy level of the magnitude of the CVD issue. There are several dimensions of this lack of awareness, which translate into a lack of will to enact the appropriate measures. An understanding of these dimensions is crucial as it opens doors to means of time-efficient and locally relevant advocacy. Firstly, CVD is not identified with the health care priorities of the region, where a focus on communicable, nutritional and reproductive health issues has traditionally prevailed for decades. This is further complicated by the multilateral and bilateral donor policies which continue to prioritize on these issues. Whereas these health problems are an important part of the *unfinished health agenda* in poorer countries, lack of attention to non-communicable diseases (NCD), especially CVD, is bound to have grave implications. Secondly, prevention of major NCD is also not identified as being part of primary health care, whereas they qualify to be within that framework by any standard applied. These two issues need to be addressed at the policy level in order to make a significant headway.

A major opportunity in this context can be identified through the role that international health organizations, multilateral and bilateral donors and economic development agencies can play in setting the health care agendas in these countries. These organizations contribute a significant share towards the public sector health development expenditure; they have and will continue to play a major part in setting the health care priorities of developing countries. This opportunity has the potential to replace traditional advocacy time efficiently.

Synergism with development initiatives

Opportunities can also be identified in the framework of development initiatives in South Asian countries. These initiatives are driven largely by pro-poor policies and therefore it makes sense to highlight the economic impact of CVD. CVD has severe economic consequences that result from premature death and prolonged disability.^{cxxiii} Study of the expatriate South Asian coronary risk has revealed that South Asians have a higher age-adjusted mortality as compared to Europeans.^{cxxiv} It needs to be additionally recognized that CVD is not confined to the rich; while the affluent may be the first in developing countries to adopt deleterious lifestyles, and initially suffer high rates of CVD, in later phases, the epidemic rates are especially high in the poorest and least educated populations.^{cxxv} In addition, management of CVD requires significant out of pocket expenditures over prolonged periods of time. These expenditures are substantial when matched against household incomes with disastrous economic effects for poorer groups, especially women and children in the household. Additionally, poor patients with CVD are likely to be marginalized and their increasing numbers, as the CVD epidemic matures, will in all probability lead to huge inequalities in South Asian health care.

In the context of the development sector's "gender focus" it needs to be recognized that the CVD death toll is not limited to men. Data in the developed world setting shows that while CVD mortality rates are lower in women, 30-69 years of age than in men, they still exceed the mortality rates of every other cause of death.^{cxxiii} In terms of total deaths CVD have claimed the lives of more females than males. Despite this grim picture, most women are far more afraid of breast cancer than of CVD even though CVD have been reported to cause almost 1 in 2 deaths in women while breast cancer causes 1 in 28 women deaths.^{cxxvi} It has been demonstrated from the study of coronary risk in South Asian expatriate women that the sex difference in coronary mortality is narrower than in Europeans so that some of the immunity of women from CHD is lost in South Asian populations.^{cxxvii} When extrapolated to the native setting this has serious implications in view of the limited opportunities that women have to access care in a gender-biased culture. This highlights the need to prioritize prevention and to consider women's health beyond the definition of reproductive health.

In the development sector, several policy and implementation frameworks are geared to strengthen health systems and improve the quality and coverage of maternal health care with reduction in maternal mortality as the outcome target. In this context it needs to be recognized that one third of maternal mortality is attributable to pregnancy-induced hypertension. Clearly a lifestyle modification approach integrated with reproductive health care will be invaluable to meet this target and will also open the doors to an effective community wide health promotion initiative.

The identification of the overall CVD impact on the under-privileged communities therefore makes the case to highlight CVD prevention as being directly synonymous with the pro-poor development policies with a view to engaging the development sector in this effort.

Opportunities for intervention at the programme level

Policies to promote CVD prevention in South Asia need to consider the existing health care delivery channels and identify opportunities within the system. By western standards most South Asian public health systems are ill equipped and under funded to implement comprehensive CVD control polices. However, there are several channels that are unique to the South Asian health systems. Over the decades extensive population welfare activities, communicable disease control programmes, vaccination campaigns and poverty reduction activities in the rural and urban underprivileged areas have created networks at the grassroots level with significant outreach. These existing and operational networks integrate public and private sector health services directly and indirectly with the community. These channels can be effectively used not only for CVD health promotion but also for population-wide screening programmes as in the case of blood pressure screening with favorable cost and logistic implications; this approach offers an alternative to independent vertical programmes for CVD control in the face of resource constraints. Such programmes in the public and the private sector are supported through the financial participation of international development agencies. Clearly a policy shift that favors the integration of the CVD prevention approach can be most useful in this regard.

Several other opportunities can be useful with regard to CVD health promotion in South Asia. The influence of locally influential personnel as in the case of feudal lords and tribe's chiefs can be seen as an effective means of inculcating behaviour change within their own populations. Fewer newspapers read by almost all social classes ensure a higher penetration, unlike developed countries where class and education segregation make the newspaper print far more diverse and not as efficient in terms of penetration. The presence of fewer electronic media channel options translates into a higher viewership of a single channel and therefore a higher penetration of messages. In this context, the public sector control on the media can be seen as a potentially effective opportunity.

The prevention research agenda

There are basic issues around cardiovascular research that make research agendas unbalanced and biased towards therapy and technology. Relating to risk factor research, it is important to realize that the epidemiology of diseases is based on studies carried out only on 20% of the world's population confined to the western world. This is particularly relevant in the context of the South Asian CVD risk and has already been alluded to in the section on epidemiology. CVD research in this region should build on existing prevalence surveys and should in addition, prioritize on implementation research that evaluates feasible interventions. Necessary infrastructure support and local capacity building for research is crucial to these approaches.

The role of health professionals

On the population level, health professionals can play a crucial role in influencing lifestyle decisions in poor countries. Their influence as local advocates places their role beyond their clinical capacities and extends to the population in general. It needs to be recognized that majority of the health care delivery in remote rural areas in the region is through formally and informally trained and traditional health professionals; it is imperative to include them in the module to maximize the impact at the grass roots level. Confining involvement to lifestyle and behavior change and population-wide screening measures may obviate ethical issues around such an approach.

There can be several approaches to engage health professionals in CHD prevention. One such approach focuses on drawing professionals into the prevention loop through opportunistic screening programmes. Blood pressure screening is perceived by the public as well as the providers as meeting a recognized 'clinical' need. Therefore, it elicits a stronger motivation and draws together a coalition of health professionals from diverse disciplines along with the public. The programme is unlikely to encounter the powerful resistance of organized vested interests as, for example, a tobacco control programme would. Since risk reduction at every level of elevated blood pressure envisages 'comprehensive cardiovascular disease risk reduction' as the goal, hypertension control would also be a vehicle for dietary control, tobacco control, diabetes control and obesity control. Thus, it would open the door for effective multi-pronged community intervention for CVD control.^{cxviii}

Health professionals should be the target for specific training with regard to CVD prevention both at the population and the clinical level. At the clinical level it needs to be recognized that physicians in South Asia usually do not have the support of related health professionals such as dietitians and the support services of specialized anti-smoking, weight reduction and diabetic clinics, as is the norm in the developed world. Professional training at all levels should therefore address this need with curricula introduced for physicians and health professionals during the course of formal and informal training. To maximize the impact of training, *train the trainers* approach may be adopted for promoting CVD prevention at the professional level.

Training must also focus on the provision of evidence-based, cost-effective and above all affordable care. Analysis of cost of therapeutic packages viewed against household incomes and out of pocket health expenditure reveals that several packages are unaffordable for the vast majority of the population (Appendix A). This would adversely affect the compliance of patients with their prescribed care. It is therefore relevant to grade recommendations based on cost and individual affordability. Such an approach may raise ethical issues but given than the circumstances it can be argued that not issuing such guidelines will also be unethical since the ideal option would be unaffordable for the vast majority; identifying such efforts in the cost-effectiveness dimension can also mitigate these concerns.

The current information and communication technology (ICT) boom can play a significant role in advancing the prevention agenda in South Asia to target the group of health professionals with access to this facility. Though of limited use in the larger context, it can play a significant role amongst the key players to create awareness of the magnitude of this issue, to disseminate data, and facilitate training.

Risk factor modification in South Asia

In any population, majority of the individuals have moderate levels of risk factors. Together those at moderate risk contribute more to the total burden of disease than those at the higher end. This highlights the need to address risk factor modification at the population level through the primary⁸ and the primordial⁹ prevention approaches rather than focus on the high-risk approach alone. The largest proportion of CVD events is also known to occur due to a combination of moderate elevations of many risk factors. The role of risk interaction should also be emphasized for the South Asian population, in view of the higher prevalence of risk clustering in this ethnic group.

In South Asia where the challenges of addressing CVD are serious, primordial prevention should feature prominently as part of the CHD prevention strategy, preserving lifestyles in the rural areas and preventing the introduction of changes that have the potential to accelerate rates of CHD in the region. The other priority should involve the population-based primary prevention approach that aims to decrease the population levels of common CHD risk factors. Studies on other Asian populations have indicated that a 2% reduction of mean blood pressure has a potential to prevent 1.2 million deaths from stroke and 0.6 million from CHD every year;^{cxxix} clearly this approach is logical for the vast populations of the South Asian region.

Population goals should therefore focus on lifestyle interventions centered on cost effective approaches involving dietary modification, tobacco use cessation, physical activity, weight loss and stress management. The

⁸ Guidance given to individuals with known risk factors but without established CHD

⁹ Prevention of the acquisition or augmentation of risk factors or preserving risk factor free societies from the penetration of risk factor epidemics

population-wide approach should also encompass screening for high blood pressure where possible.

In the South Asian context guidelines and recommendations, both for the clinical and public health approaches need to be different from those that are developed in other settings because of cultural considerations and resource constraints. Several issues need to be recognized in this context. Clinical guidelines for the South Asia region need to be clear, simple, user-friendly socio-culturally customized with an explicit set of options for major decisions, supported by current and valid recent evidence, in a simple and accessible format and also need to be flexible to meet the needs of individual patients. Whereas concerns relating to flexibility in the developed world largely center on patients being able to determine their own course of treatment according to their own values, in South Asia they stem from economic issues. Thus the application of the same guidelines to technology-laden tertiary care units, and to remote rural health care units without a serving road or electricity, several hours away from the nearest coronary care unit is a challenge. Cost is a major factor for compliance in South Asia where health insurance is virtually nonexistent and most expenses are borne by patients out of pocket. This has necessitated the inclusion of a cost-based approach to the therapeutic recommendations in order to facilitate treatment choices according to the resources at hand.

Dietary recommendations for the South Asian population need to be culturally specific and need to cater to the feasibility of modifications in view of what is available, acceptable and affordable. The South Asian diet is significantly different from the western diet for which healthier modifications have been developed extensively. A heart healthier version of the South Asian diet has been developed and is appended to this document (Appendix B). Variation in the dietary patterns of populations in different parts of South Asia have been taken into consideration while drawing up these recommendations. This dietary guideline should be used as a baseline framework for individual regions within countries with diverse dietary patterns to expand on.

Cut off values for BMI need to be lower in this population; emerging data from the “INTERHEART Study” suggests that in South Asians, increases in BMI from 22 to a range of 23 to 25 is associated with a 30% increase in cardiovascular disease^{CXXX} and therefore lower BMI cut off points have been

recommended. Cut off values for waist circumference also need to be lowered in view of the average height of individuals in the South Asian subcontinent which is about 1.7 m for men and 1.58 m for women in urban settings and about 2.5 to 5 cm shorter in rural settings; based on this data cut off points for waist circumference have been lowered to 91.5 cm in men and 84 cm in women.

Recommendations on smoking cessation in South Asia need to take into consideration the different forms in which tobacco is used in the subcontinent in addition to cigarettes; it is therefore appropriate to refer to “tobacco use” rather than “smoking” both at the public health and clinical levels. This includes cigarette smoking, smoking of local forms of tobacco such as the hukka¹⁰, beeri¹¹ and chewable smokeless tobacco. Recommendations on tobacco use cessation should address this issue.

Physical activity and weight reduction offer the greatest opportunity for intervention in these cultures and indeed in any culture. Physical activity should however be encouraged for women in Muslim cultures in an environment and form that respects religious proscriptions. Recommendations with regard to CHD in women have been addressed under a separate heading to emphasize this unrecognized issue; this also includes certain aspects of risk factor management that are unique to women.

Increased serum cholesterol should be recognized as an important risk factor for CHD but should be taken in the context of other risk factors such as smoking, raised blood pressure and physical inactivity. It should also be recognized that blood cholesterol alone is a relatively poor predictor of individual CHD risk. The majority of CHD events occur in people with average or low blood cholesterol levels. Consequently, cholesterol screening at a population level is not recommended.^{CXXXI} The need to highlight this in the South Asian context is an important element of the prevention-based approach to CHD.

¹⁰ Device for smoking tobacco which is like the middle eastern “hubble bubble”; tobacco is heated in a pot and is made to pass through water cisterns before being inhaled through a long tube; used for communal smoking.

¹¹ Beeri is a local form of cigarette in which tobacco is rolled in a leaf.

As part of the high-risk population approach, individuals should be identified on the basis of easily identifiable markers for targeted screening for hypercholesterolaemia and diabetes. These markers may include obesity, family history, the presence of other risk factors and CVD. Recent studies have also identified that the simultaneous measurements and interpretation of simple variables, such as waist circumference, could be used as inexpensive screening tools for the identification of men at risk for CVD;^{lxv} this may be particularly relevant for South Asians. The most effective way to reach such groups is to complement the population-wide health promotion strategies with carefully targeted messages interlinking them with locally available health services.

FRAMEWORK RECOMMENDATIONS

Framework policy recommendations

- ? At the macro policy level the need to identify CVD prevention as part of the primary health care package should be recognized and given due priority alongside reproductive and nutritional health and communicable diseases.
- ? CVD prevention should be seen as being synergistic with poverty reduction strategies, and addressed in development initiatives.
- ? Policy changes should integrate heart health with communicable disease, reproductive health and population control programmes in an attempt to create cost and time effective opportunities for prevention.
- ? Policy change with respect to CVD must include relevant areas in the domains of food and nutrition, tobacco, agro-industrial diversification, urban planning, education and rural development.
- ? Policies relating to food and nutrition should ensure availability, favorable pricing, and labeling of heart healthy food.
- ? Policy issues regarding tobacco should be dealt with in two stages. Initial priorities should focus on goals that are realistically achievable in the short to medium term, such as imposing constraints on advertising and sale to minors, displaying statutory warnings on labels and legislation to ban smoking in public places and transport utilities. Subsequently major issues should be addressed such as agro-industrial diversification favoring tobacco substitution, and transnational marketing of tobacco, which may affect pricing, production and taxation.
- ? Policy changes should address transport, urban planning and neighborhood development to promote physical fitness and provide tax incentives for exercise equipment. Policy changes to promote worksite

physical activity should consider flexible working hours and worksite exercise facilities.

- ? Policies should ensure the availability of effective drugs, devices and procedures at affordable prices to be used in a cost-effective manner.

Framework programme recommendations

? **Public health**

- ? Culturally and linguistically appropriate and effective community health promotion and disease prevention programmes should be encouraged and made available; if they already exist they should be strengthened and integrated with the formal health care sector.
- ? Cardiovascular disease prevention should be integrated with primary health care.
- ? Cardiovascular health education should be integrated with other health promotion initiatives.
- ? The public health approach should target population-wide lifestyle interventions, population-wide screening for high blood pressure and screening of the high-risk group for diabetes and hypercholesterolaemia.
- ? Lifestyle advice should center on tobacco use cessation, weight control, a heart healthy diet, physical activity and stress management.
- ? Cardiovascular health promotion should be part of the national media strategy.
- ? Cardiovascular health should be addressed in school based health education and/or as part of the science curriculum.
- ? Cardiovascular health education should be offered in places of religious worship and worksites where appropriate.
- ? Infrastructure support and local capacity building for research should be prioritized.

? **Clinical**

- ? Cost-effective and customized diagnostic and management algorithms should be developed for the treatment of all common cardiovascular diseases. These guidelines should be made widely available in the region.

- ? The availability of effective and affordable drugs, devices and procedures should be ensured.
- ? Referral chains should be established which should provide effective links between primary, secondary and tertiary health care centers whenever required.
- ? “Train the trainers” approach should be adopted for promoting CVD prevention at the professional level.
- ? All physicians must commit the time to make a proper assessment and initiate preventive efforts. Physician’s advocacy of healthy habits including tobacco-use cessation, healthy eating, weight control, and physical activity should be universal.
- ? Physicians in South Asia usually lack support of related health professionals such as dietitians and the support services of specialized anti-smoking, weight reduction and diabetic clinics, as is the norm in the developed world. Therefore a customized risk management curriculum should be introduced for physicians and health professionals during the course of formal and informal training.
- ? Specialist opinion should be sought whenever essential and feasible. The cut-off points for specialist referral for every risk category should be recognized.

P RIMORDIAL PREVENTION

The major thrust in the prevention of atherosclerotic and hypertensive heart diseases over the last two decades has been the detection and control of their risk factors, whereas the prevention of risk factors themselves has not received much attention.^{cxxxii} “Prevention of the acquisition or augmentation of risk factors” is distinct from risk factor “detection” and “management” (constituting primary prevention) and is the concept of “primordial prevention” coined by Strasser^{cxxxiii} in 1980 meaning “preserving risk factor free societies from the penetration of risk factor epidemics”. In South Asia where the challenges of addressing CVD are serious, primordial prevention should feature prominently as part of the CHD prevention strategy, preserving lifestyles in the rural areas and preventing the introduction of changes that have the potential to accelerate epidemic rates of CHD in the region.

Such interventions are effective both in early life and later; as the risk factor incidence continues well into the later years; interventions should therefore, ideally cover the entire lifespan of populations. School health programmes, which are crucial in targeting behavioural change in childhood, should therefore be complementary to the adolescent education programmes and the media advice targeting adults. Rural communities in the SAARC region, constituting more than 60% of the population, are likely to be the prime beneficiaries of the primordial prevention approach as they have not, as yet been exposed to the influences and risks that are part of urbanization and acculturation.

Goal:

- ? Preserving entire risk factor-free societies from the penetration of risk factor epidemics

Recommendations:

- ? Primordial prevention should be recognized as a priority at the policy and programme level, with the necessary investment of resources.
- ? Refer to the programme framework recommendations.

P RIMARY PREVENTION

Primary prevention refers to guidance given to individuals with known risk factors but without established CHD. Primary prevention involves population level prevention and encompasses both population goals and treatment of risk factors in individuals without established CHD through the public health and the clinical approaches. Whereas the public health approach targets both the general population and the high-risk group, the clinical approach gives physicians the opportunity to detect the presence of established risk factors and to reinforce lifestyle changes and prescribe drug therapy if required to modify these risk factors in an attempt to avert the intensification of these risk factors and consequent CHD. The emphasis in this section will be on modifiable risk factors.

TOBACCO USE

Public health approach

- ? The use of tobacco rather than “smoking” should be taken into account. This includes cigarette smoking, smoking of local forms of tobacco (‘hukka’, ‘beedies’ and chillums) and chewable smokeless tobacco. These should be referred to as cigarette and other forms of tobacco (COT) use.
- ? Counseling for COT cessation should be universal for all health encounters.
- ? Misconceptions relating to local forms of tobacco use, as being relatively harmless should be addressed.
- ? Passive smoking should be addressed alongside COT use wherever appropriate; passive smoking should also be addressed as part of the health promotion component of reproductive health initiatives with reference to its implications for the health of the newborn.

- ? Physicians and all other health professionals, institutions and professional organizations should collaborate actively to support smoking cessation programmes.
- ? Customized self-help materials assisting with smoking cessation should be developed.
- ? Refer to framework recommendations.

Clinical approach

Goal: cigarette and other forms of tobacco-use cessation.

Screening: all patients and their families.

Recommendations:

- ? The present and past status of COT use, and exposure to passive smoking should be determined and quantified.
- ? Counseling for COT use cessation should be universal and reinforcement of the non-smoking status of patients and their families should preferably be a part of every evaluation.
- ? Referral to published material and smoking cessation programmes where applicable and accessible should be encouraged and facilitated.
- ? Physicians in general and cardiovascular physicians in particular should be familiarized with Nicotine Replacement Therapy (NRT). Where cost, comprehension and availability is not an issue; NRT should be offered to patients and monitored.

PHYSICAL ACTIVITY

Goal: accumulation of equal to or more than 30 minutes of moderate intensity physical activity on most, preferably all days of the week.

Screening: all individuals.

Recommendations:

- ? A minimum of 30 minutes of moderate intensity dynamic exercise should be recommended to all individuals; this may be performed in intermittent shorter bouts (e.g. 10 minutes). Examples of such recommended activity are, brisk walking, jogging, bicycling or walking instead of using the car, etc.
- ? Recommendations on physical activity should take into account cultural norms and sustainability.

- ? Physical activity should be encouraged for women in Muslim cultures in an environment and form that respects religious proscriptions. Support from Islamic religious leaders is crucial in endorsing the need for more exercise and in encouraging full participation of women in Muslim cultures.

WEIGHT

Goal:

- ? BMI lower than 23.
- ? Waist circumference less than 91.5 cm in men and 84 cm in women.

Screening:

Where facilities exist and there are no time constraints, ideally, measurement of the patients' weight, height, waist and hip, and calculation of BMI and waist hip ratio should be carried out at least once. When time constraints prohibit this, measurement of the waist should be carried out and the patient weighed at least once.

Recommendations:

- ? Waist circumference should be used as an inexpensive screening tool for the identification of men at high risk of CHD.
- ? It should be recognized that overweight and obesity are associated with insulin resistance and the metabolic syndrome,¹² the risk factors of the metabolic syndrome are highly concordant and that the prevalence of the metabolic syndrome is high among South Asians.
- ? Weight management should begin with a low calorie diet (Appendix B) and physical activity.

DIET

- ? All individuals should be encouraged to adhere to the Heart Healthy Eating Plan for South Asians (Appendix B).
- ? Patients who drink alcoholic beverages should be advised to restrict their intake to two drinks per day. Patients who do not drink should have this choice reinforced.

¹² According to the ATP 111 guidelines, the diagnosis of the syndrome is made when three or more of the following risk determinants are present: waist circumference more than 102 cm in males and 88 cm in females, TG >150 mg/dl, HDL cholesterol <40 in men and <50 in women, blood pressure >130/85 mm hg and fasting blood glucose >110 mg/dl. The cut off values for waist circumference have been lowered for the South Asian population based on the unpublished results of the INTERHEART data for the South Asian ethnic group.

- ? All individuals should be advised to restrict their daily salt to less than 6 grams per day (moderate use of salt in the curry, no added salt to the staple bread, no added salt at the table and no commercial pickles and chutneys).

STRESS

- ? Depression, elevated levels of depressive symptoms, anxiety, low social support, hopelessness, anger, hostility and stress at work should all be recognized as risk states for CHD.
- ? It should be recognized that these attributes can also negatively influence behaviourally alterable risk factors such as smoking, exercise and diet as well as patients' tendencies to comply with recommended medications or to respond to symptoms by seeking medical treatment.
- ? Counseling for stress in the context of CHD prevention should be routinely practiced and stress-relieving techniques that are religiously and culturally acceptable, advocated.
- ? For severe symptoms, referrals to a psychiatrist, or in case where one is inaccessible, appropriate medication should be advised.

HIGH BLOOD PRESSURE

Public health approach

- ? It should be advocated that the beneficial effects of lowering blood pressure extend beyond preventing coronary heart disease to also preventing stroke.
- ? High blood pressure screening and control should be considered as the ideal "entry programme" of an integrated CVD control strategy in the SAARC countries. All individuals should have their blood pressure checked once a year after the age of 30. Those with normal blood

pressure should be encouraged to have their blood pressure checked every year.

- ? Population-wide screening should be the goal of Hypertension Detection Programmes in view of the high prevalence of high blood pressure in the South Asia. Where not feasible due to scarcity of resources, screening of the high-risk population should be considered a matter of priority, with formal screening programmes including and screening advice targeted to men and women aged 45 years and above, those with generalized and central obesity, a strong family history of hypertension, stroke and sudden premature death in the immediate family or a combination of these factors.
- ? Opportunistic screening involving all categories of health care providers using any health care encounter to screen patients or individuals living in a community for hypertension should be prioritized.

Clinical approach¹³

Goal:

- ? Less than 140 mm Hg systolic and 90 mm Hg diastolic.
- ? Less than or equal to 130 mm Hg systolic and 85 mm Hg diastolic in renal insufficiency or diabetes.

Screening:

- ? Initial evaluation of patients with high blood pressure should be inclusive of a thorough history and physical examination, with only a limited number of routine investigations.
- ? Once confirmed, the aim of evaluation for high blood pressure should be to elicit and document the 8 “C”s. 1) the *causes* of secondary hypertension where curative therapy may be targeted; 2) *contributory* factors where aggressive modification may be beneficial in terms of medication-free or low cost control; 3) the *complications* of hypertension; 4) the presence of additional *cardiovascular risk factors*, crucial for risk categorization; 5) *contraindications* to specific drugs; 6) *co-morbid* conditions which influence choice of medication; 7) *cost considerations* which may affect long-term compliance and 8) patient *categorization* for drug therapy.

¹³ The cut-off values for therapy have been based on the Sixth Report of the Joint National Committee on the Prevention, Detection, Evaluation and Treatment of High Blood Pressure.

- ? Routine investigations
 - ? Where cost is not an issue: urine test for protein and blood, serum creatinine and electrolytes, blood glucose and serum total cholesterol, triglycerides, LDL and HDL cholesterol and ECG.
 - ? Where cost constrained, urine for protein initially, and blood glucose, cholesterol and ECG only if clinically warranted.

Recommendations:

- ? Lifestyle advice given to *all* hypertensive patients should be clear on two issues: *lifestyle interventions can reduce the need for drug therapy and enhance the effect of antihypertensive agents*. Therefore encourage weight reduction, reduction in salt intake to ≤ 6 g/day (do not add salt to food at the table and avoid pickles), reduction in fat intake, limitation of alcohol consumption ≤ 21 units/week in men and ≤ 14 units/week in women, regular dynamic exercise and increase in fruit and vegetable consumption to 7 portions per day. And that *lifestyle interventions can reduce the overall cardiovascular risk*. Therefore encourage patients to quit smoking, reduce their saturated fat intake and substitute it with polyunsaturated, monounsaturated fats and oily fish and be physically active.
- ? Patients with high normal blood pressure 130-139/85-89 mm Hg.
 - ? No or one risk factor (not including diabetes): lifestyle modification.
 - ? Multiple risk factors (high-risk population) and diabetics: drug therapy along with lifestyle modification.
- ? Patients with stage 1 hypertension: 140-149/90-99 mm Hg.
 - ? No risk factors: lifestyle modification up to 12 months.
 - ? 1 risk factor (not including diabetes): lifestyle modification up to 6 months.
 - ? Multiple risk factors and diabetics: drug therapy along with lifestyle modification.
- ? Patients with stage 2 hypertension: ≥ 160 systolic and or ≥ 100 diastolic, should be given drug therapy under all circumstances along with lifestyle modification.
- ? Prescribing anti-hypertensive therapy
Appendix A tabulates the monthly cost of various anti-hypertensive drugs; for each drug within a class the minimum effective and the ceiling recommended dosage has been listed. For both, the monthly minimum

and maximum cost packages available in the market have been calculated; these costs have been viewed as a percentage of the monthly rural and urban household incomes and as a percentage of the monthly household health expenditure by the private and the public sector. The cost of anti-hypertensive medication differs in the various SAARC countries, overall the cost variability being highest in Pakistan. The appended cost calculation is intended to give the prescribing physician an overview of the health economic impact of long-term anti-hypertensive therapy with implications for compliance and disease morbidity. Cost of therapy should be visualized as a major consideration in the management of high blood pressure and therefore, the following recognized:

- ? Option 1, Ideal: Where cost is not a consideration, or where patients are sure to be reimbursed for their medical expenses, the protocol given in Table 2 is recommended. In this situation the choice of antihypertensive medication is an individualized decision. In uncomplicated hypertension, pharmacological therapy should begin with beta-blockers or diuretics. It should however be recognized that there are compelling indications for specific agents in certain clinical situations.

Table 3 *compelling indications and contraindications for various anti-hypertensive drugs.*

Drugs	Compelling indications	Compelling Contraindications
Diuretics	First line therapy unless other compelling indications	Gout
Beta blockers	Myocardial infarction Angina	Asthma Heart block
ACE Inhibitors	Heart failure LV dysfunction Post myocardial infarction	Pregnancy Bilateral renal artery stenosis
Calcium Antagonists (Dihydropyridine)	Elderly Isolated systolic hypertension	
Calcium antagonists (Rate limiting)	Angina	Heart block Heart failure
Alpha Blockers	Prostatism	Urinary incontinence

Angiotensin II Antagonists	As for ACE inhibitors; use if ACE inhibitors are contraindicated.	As for ACE inhibitors; use if ACE inhibitors are contraindicated.
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- ? Option 2, low cost: where cost constraints make long-term compliance unlikely or where patients benefit from charitable relief over an extended period of time, beta blockers and diuretics should be prescribed unless there are pressing contraindications, or where the presence of other co-morbid condition(s) makes the choice of another drug a matter of priority. Beta blockers and diuretics have been shown to be the most cost-effective drugs.^{cxxxiv} In indirect comparisons between beta blockers, diuretics and newer ACE inhibitors and calcium channel blockers there was no evidence that the newer drugs were associated with fewer side effects.^{cxxxv} The other approach to ensure long-term affordability involves calculation of the total monthly prescription cost of medication taken by an individual; this should be less than 5% of the monthly per person household income. It is also recommended that all physicians should familiarize themselves with ranking of drugs according to their cost within classes, so that one automatically becomes the preferred option in the group being the cheapest.

DYSLIPIDAEMIA

Public health approach

Increased serum cholesterol should be recognized as an important risk factor for CHD but should be taken in the context of other risk factors such as smoking, raised blood pressure and physical inactivity. It should also be recognized that blood cholesterol alone is a relatively poor predictor of individual CHD risk. The majority of CHD events occur in people with average or low blood cholesterol levels. Consequently, cholesterol screening at a population level is not recommended.^{cxxxvi}

- ? Targeted screening or screening of the high-risk population should be the goal. This involves checking for high cholesterol levels in patients identified on the basis of clinical markers such as the presence of hypertension, obesity, or a family history of coronary or cerebrovascular disease.

- ? In those identified for screening, a complete lipoprotein profile (total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides) is the preferred initial test.
- ? The Heart Healthy Eating Plan for South Asians should be promoted for all adults (Appendix B).

Clinical approach¹⁴

Goals:

- ? Total cholesterol less than 200 mg/dl
- ? LDL cholesterol (LDL)
 - ? less than or equal to 160 mg/dl, if 0-1 risk factors
 - ? less than 130 mg/dl, if 2 or more risk factors
 - ? less than 100 mg/dl if diabetic
- ? High triglycerides
 - ? Triglycerides less than 150 mg/dl
 - ? Prioritize goals for LDL lowering
 - ? Management of the metabolic syndrome

Screening:

- ? Patients in whom there is a possibility of secondary causes as in patients with renal disease, hypothyroidism and liver failure should be screened at least once during the course of these illnesses.
- ? Patients with xanthomata or a family history of early CHD with a genetic dyslipidaemia should have screening once at detection of disease and once again when over the age of 30, and if normal 5 yearly thereafter.
- ? Patients with other risk factors for cardiovascular disease, at least once.

Recommendations:¹⁵

- ? Dietary advice for cholesterol lowering should be routinely given as part of the first evaluation and reinforced during subsequent visits.
- ? The use of *Isphagula*, which is effective in cholesterol lowering by 10-15% and is traditionally used in the subcontinent, should be recommended.
- ? Dietary therapy: LDL based cut off points for reinforcing the Heart Healthy Eating Plan for South Asians should be recognized; it should additionally be noted that these are *not* cut off points for the institution of drug therapy.

¹⁴ Therapeutic goals have been based on the Adult Treatment Panel III Guidelines

¹⁵ Risk factors not including diabetes, for diabetes in the primary prevention setting, refer to the section on diabetes

- ? LDL greater than 160 mg/dl, if 0-1 risk factors
 - ? LDL greater than 130 mg/dl, if 2 or more risk factors
 - ? LDL greater than 100 mg/dl if diabetic
- ? Patients in whom dietary therapy fails should be considered for drug therapy if long-term affordability is not an issue and they are at a particularly high risk of CHD events based on their total risk profile.
- ? Drug therapy: The decision to use drug therapy to control risk factors depends on a balanced assessment of absolute risk and the efficacy, safety, cost-effectiveness, and long-term affordability of the intervention. The monthly cost of various lipid-lowering medications, when taken as a percentage of the monthly household incomes in the urban and the rural areas and the health expenditure by the private and the public sector is appended (Appendix A). It is evident that lipid-lowering therapy would be unaffordable for the vast majority of the population in the region. Use of cholesterol-lowering drugs for the prevention of CHD should depend heavily on the assessment of absolute risk; drug therapy should be used cautiously for primary prevention in young adults who are otherwise at low risk. It should be recognized that in asymptomatic people who are at high risk of CHD, the costs of lowering cholesterol, using statins are high relative to the benefits. It should be recognized that cholesterol lowering is one of a number of methods of reducing the risks of CVD. The other equally important methods are smoking cessation, physical activity, control of hypertension and weight reduction in the overweight. It should also be recognized that the cost effectiveness of some anti-hypertensives, aspirin and beta blockers is greater than statins. Greater priority should therefore be given to the appropriate use of other drug treatments. Before considering the use of lipid lowering drugs, other methods to reduce the risk of coronary heart disease (CHD) should be actively instigated; these include advice and help on COT use cessation, dietary advice to control weight and lower lipids and advice on regular physical activity.
- ? Where cost is not a consideration therapy should be based on specific LDL, HDL and TG cut of points.

LDL:

- ? LDL cut off points for the institution of pharmacological therapy should be recognized; these are:
 - ? LDL greater than 190 mg/dl, if 0-1 risk factors
 - LDL greater than 160 mg/dl if 2 or more risk factors
 - ? LDL greater than 130 mg/dl if the risk is very high
 - ? Therapy with LDL lowering should be targeted to people who are at high risk of CHD rather than based upon cholesterol levels alone.
- ? Triglycerides:
 - ? The importance of high triglyceride levels and low HDL levels should be emphasized for the South Asian population.
 - ? Borderline high triglyceride levels, 150-199: weight reduction and physical activity.
 - ? High triglyceride levels, 200-499: weight reduction, physical activity and drug therapy to lower LDL to the desired limits with LDL lowering drug, or by adding fibrates.
 - ? Very high triglycerides: very low fat diet (less than or equal to 15% of the caloric intake, weight reduction, increased physical activity and triglyceride lowering drug (fibrate or nicotinic acid). Only after triglyceride levels have been lowered to less than 500 mg/dl should attention turn to LDL lowering.
- ? HDL:
 - ? For low HDL ≤ 40 mg/dl, follow guidelines for LDL lowering, emphasize on weight reduction and increase in physical activity particularly when in association with the metabolic syndrome.

DIABETES

Public health approach

- ? Population-wide screening for diabetes in all adults over the age of 35 years in combination with the assessment of their positive and negative risk factors is theoretically ideal; however, realistically:

- ? Targeted screening or screening of the high risk population should be the goal which involves checking for blood glucose levels in patients identified on the basis of clinical markers such as the presence of hypertension, generalized and central obesity.

Clinical approach

Goal:

- ? Fasting blood glucose level of less than 120 mg/dl
- ? Therapeutic goal of blood pressure lowering is 130/85 mm Hg
- ? Therapeutic goal of LDL lowering is <100 mg/dl

Screening:

- ? Fasting blood glucose should be measured in all individuals with more than two risk factors for CHD.

Recommendations:

- ? All diabetic COT users should be made aware of the fact that they are up to four times more likely to suffer from cardiovascular death than non-smokers, and hence strongly discouraged from smoking.
- ? Patients should be encouraged to actively participate in their treatment.
- ? ACE inhibitor therapy and diuretics should be prioritized as anti-hypertensive agents.
- ? All patients should have their lipid levels checked and should be managed according to the recommendations given in the relevant section.
- ? Initiate LDL lowering drugs when LDL cholesterol >130 mg/dl. When LDL is 100-129 mg/dl, exercise clinical judgment to initiate therapy. Manage triglycerides as discussed in the section on triglycerides under dyslipidaemia.

DRUG THERAPY

- ? Low dose Aspirin (75 mg) should be given to treated hypertensive patients whose blood pressure is well controlled and in men with particularly high CHD risk. Aspirin or other platelet modifying agents should not be routinely indicated in the management of high-risk individuals.
- ? Empirical vitamin supplementation with folic acid and vitamins of the B complex series should not be recommended at the cost of other essential medication.
- ? Drug therapy for high blood pressure and dyslipidaemia should be advised as indicated in the relevant sections.

NOVEL RISK FACTORS

- ? Screening and management of novel risk factors such as homocysteine, coagulation factors, platelet reactivates, Lp(a) and markers of infection should not be pursued.

WOMEN

- ? Risk management strategies for women should be as aggressive as in men.
- ? Although general recommendations apply to both men and women, certain aspects of risk factor management that are unique to women should be actively addressed. During pregnancy, complete COT use cessation, avoidance of excess weight gain, and avoidance of food rich in fat should be promoted.
- ? Women with diabetes should have tighter control of diabetes, as diabetes is a more powerful risk factor in women (3-7 fold compared to 2-3 fold in men).
- ? The rising trend of smoking amongst women in the region should be strongly discouraged.
- ? With the increasing emphasis on population control in the region, it should be recognized that the use of low dose oral contraceptive birth control preparations should largely be confined to women less than 35 years of age, who do not smoke and who do not have hypertension.
- ? Women who are unable to remain physically active outside of their own homes due to cultural constraints should be encouraged to remain active at home while reinforcing the importance of physical activity.
- ? Hormone Replacement Therapy (HRT) should not be primarily used for reduction in CHD risk.

ECONDARY PREVENTION

Secondary prevention is the modification of risk factors in patients with CHD to prevent the further recurrence of such events. These guidelines apply to all those who have any form of CHD such as a prior myocardial infarction, stable and unstable angina and those having undergone coronary artery procedures such as coronary artery bypass grafting and angioplasty or stenting procedures.

TOBACCO USE

Goal: complete COT use cessation

Screening: all patients with CHD

Recommendations:

- ? COT use cessation should be a priority in CHD patients. Advice should clearly state that survivors of MI who smoke, have twice the rate of recurrent infarction and cardiac death compared to those who do not smoke and that in other patients with CHD who smoke, and have not, as yet, suffered from an acute event, the chances of an acute coronary event are much higher as compared to those who do not smoke.
- ? In addition, all recommendations given under the framework of the clinical strategy as part of the Primary Prevention plan regarding tobacco-use apply here, with an emphasis that the attempt at tobacco-use cessation should be more aggressive as part of the Secondary Prevention approach.

PHYSICAL ACTIVITY

- ? Refer to the advice given as part of the Primary Prevention plan.

WEIGHT MANAGEMENT

- ? Refer to the advice given as part of the Primary Prevention plan.

DIET

- ? The Heart Healthy Eating Plan for South Asians should be recommended for all patients.

HIGH BLOOD PRESSURE

Goal: blood pressure of 130 mm hg systolic and 80 mm Hg diastolic.

Screening: all patients with CHD (the screening strategy outlined as part of the Primary Prevention plan regarding the clinical approach to high blood pressure applies here).

Recommendations:

- ? Lifestyle advice given as part of the Primary Prevention plan regarding the clinical approach to high blood pressure applies here.
- ? Drug therapy should be instituted in all cases of CHD with blood pressure levels over 130 systolic and 80 diastolic. Refer to the section on prescription of antihypertensive drugs discussed as part of the Primary Prevention plan.
- ? Betablockers need to be prioritized for the management of high blood pressure in patients that have either suffered from a myocardial infarction or suffer from angina. In the presence of any contraindication, rate-limiting dihydropyridines are the second choice. (Refer to the section on hypertension in Primary Prevention for suggested recommendations regarding the compelling indications and contraindications of other drugs).

DYSLIPIDAEMIA

Goal:

- ? Primary goal: LDL less than or equal to 100 mg/dl
- ? Secondary goals: refer to goals as discussed under primary prevention

Screening: All patients with CHD

Recommendations:

- ? All patients should be strongly advised to adhere to the Heart Healthy Eating Plan for South Asians.
- ? The first priority for lipid lowering drug therapy in patients with CHD should be patients who have had a myocardial infarction.^{cxxxvi} These patients have a very high CHD risk, and drug treatment is indicated when LDL is above 130 mg/dl. If LDL is between 100-130 mg/dl, clinical judgment needs to be exercised and drug therapy instituted only in high-risk cases where long-term affordability is not an issue. The second priority for lipid lowering therapy is in patients with angina or other clinically overt atherosclerotic disease; the same cut off points for therapy as mentioned previously for myocardial infarction apply.
- ? It should however be recognized that lifestyle modifications inclusive of a lipid lowering diet, aspirin and beta blockade should be prioritized if long-term compliance to lipid lowering therapy is unlikely because of cost considerations.

DIABETES

- ? Refer to the advice given as part of the Primary Prevention plan.
- ? Additionally; it should be recognized that diabetes is a strong risk factor for CVD; this risk is independent of the risk associated with other risk factors. It should also be recognized that diabetes confers a worse prognosis after a cardiovascular event.

DRUG THERAPY

- ? In the absence of any contraindications, long-term beta blocker and ACE Inhibitor therapy should be given indefinitely to patients with myocardial infarction.
- ? Aspirin should be prescribed to all individuals with CHD. In the presence of aspirin allergy, anticoagulation should be instituted only in patients with a prior myocardial infarction.
- ? Refer to “High Blood Pressure” in this section
- ? Refer to “Dyslipidemia” in this section
- ? Refer to “HRT” in this section

SCREENING FOR NOVEL RISK FACTORS

- ? Screening and management of novel risk factors such as homocysteine, coagulation factors, platelet reactivates, Lp(a) and markers of infection should not be pursued.

WOMEN

- ? Refer to the advice given as part of the Primary Prevention plan.
- ? It should be recognized that there are significant differences in the modes of presentation of CHD amongst men and women. These differences have important implications in the South Asian context as women have problems accessing care. It should therefore be recognized that women are more likely to have vague symptoms, and symptoms are less likely to be brought on by exercise. They are also less likely to have unrecognized infarctions and non-Q wave infarctions. Women with CHD are also more likely to be hypertensive, obese and diabetic.

HORMONE REPLACEMENT THERAPY

- ? HRT with estrogen plus progestin should not be started in post-menopausal women with established CHD. However, post-menopausal women who are already taking estrogen and progestin for over three years may continue this therapy.

SCREENING OF RELATIVES

- ? Close relatives of patients should be screened for high blood pressure, diabetes and dyslipidaemia and should receive lifestyle advice.

REFERENCE

- i World Development Indicators 2001. The World Bank, Washington, 2001.
- ii Jackson R, Feder G. Guidelines for clinical guidelines [editorial]. *BMJ* 1998;312:427-8.
- iii Thomson R, Lavender M, Madhok R. How to ensure that guidelines are effective. *BMJ* 1995;311:237-42.
- iv Woolf HS, Grol R, Hutchinson A. Potential benefits, limitations and harms of clinical guidelines. *BMJ* 1999;318:527-30.
- v Wilson A. Review on making use of guidelines in clinical practice. *BMJ* 1999;319:1078.
- vi The Canadian Cardiovascular Society 1998 Consensus Conference on the Prevention of Cardiovascular Diseases: The Role of the Cardiovascular Specialist. *Can J Cardiol* 1999;15 Suppl G.
- vii Nishtar S. Customized guidelines for cardiovascular disease prevention in South Asia. *ProCOR* [serial online] 2000 Sep 8;99:160. Available from: URL: <http://www.procor.org>.
- viii The Osaka Declaration on Heart Health 2001, Health Economics and Political Action: Stemming the Global Tide of Cardiovascular Disease. Advisory Board of the 4th International Heart Health Conference. Osaka, Japan, 2001. In press.
- ix The World Health Report 2000, Health Systems: Improving Performance. World Health Organization, Geneva, 2000.
- x World Health Report 1999, Making a Difference. World Health Organization, Geneva, 1999.

- ^{xi} Kelly DT. Our future society: a global challenge. *Circulation* 1997;95:2459-64.
- ^{xii} Murray JL, Lopez AL. Alternative projections of mortality and disability by cause 1990-2020: Global Burden of Disease Study. *Lancet* 1997;349:1498-1504.
- ^{xiii} Reddy KS, Yusuf S. Emerging epidemic of cardiovascular disease in developing countries. *Circulation* 1998;97:596-601.
- ^{xiv} Chockalingham A, Balaguer-Vintro I, editors. The impending global pandemic of cardiovascular diseases, The White Book. Barcelona: Prous Science, S.A; 1999.
- ^{xv} Haq MU, Haq K. Human Development in South Asia 1997. Human Development Center. Karachi (Pakistan), Oxford University Press; 1997.
- ^{xvi} Human Development in South Asia 2001, Globalization and Human Development. Human Development Center, Karachi (Pakistan). Oxford University Press; 2002.
- ^{xvii} Haq MU, Haq K. Human Development in South Asia 1999: Crisis of Governance. Human Development Center, Karachi (Pakistan). Oxford University Press; 1999.
- ^{xviii} Enas EA, Mehta J. Malignant coronary artery disease in young Asian Indians: thoughts on pathogenesis, prevention and therapy. *Clin Cardiol* 1995;18:131-5.
- ^{xix} McKeigue PM, Miller GJ, Marmot MG. Coronary heart disease in south Asians overseas. *J Clin Epidemiol* 1989;42:597-609.
- ^{xx} Tinker H. A new system of slavery: the export of Indian labor overseas 1830-1920. London, Oxford University Press; 1974.
- ^{xxi} McKeigue PM, Marmot MG. Mortality from coronary heart disease in Asian communities in London. *BMJ* 1988;297:903.

- xxii Klatsky AL, Tekawa I, Armstrong MA, Sidney S. The risk of hospitalization for ischemic heart disease among Asian Americans in northern California. *Am J Public Health* 1994;84:1672-5.
- xxiii Steinberg WJH, Balfe DL, Kustner HG. Decline in the ischaemic heart disease mortality rates of South Africans, 1968-1985. *S Afr Med J* 1988;74:547-50.
- xxiv Miller GJ, Beckles GLA, Maude GH, Carson DC, Alexis SD, Price SGL, et al. Ethnicity and other characteristics predictive of coronary heart disease in a developing community: principal results of the St James Survey, Trinidad. *Int J Epidemiol* 1989;18 :808-17.
- xxv Tuomilehto J, Ram P, Eseroma R, Taylor R, Zimmet P. Cardiovascular disease in Fiji: analysis of mortality, morbidity and risk factors. *Bull WHO* 1984;62:133-43.
- xxvi Hughes K, Lun KC, Yeo PPB. Cardiovascular diseases in Chinese, Malays and Indians in Singapore: differences in mortality. *J Epidemiol Community Health* 1990;44:24-8.
- xxvii Lee J, Heng D, Chia KS, Chew SK, Tan BY, Hughes K. Risk factors and incident coronary heart disease in Chinese, Malay and Asian Indian males: the Singapore Cardiovascular Cohort Study. *Int J Epidemiol* 2001;30:983-8.
- xxviii Anand SS, Yusuf S, Vuksan V, Devanesen S, Teo KK, Montague PA, et al. Differences in risk factors, atherosclerosis and cardiovascular disease between ethnic groups in Canada: the Study of Health Assessment and Risk in Ethnic groups (SHARE). *Lancet* 2000;356:279-84.
- xxix Trvelyan J, Needham EW, Halim M, Singh H, Been M, Shiu MF, et al. Evaluation of patient characteristics and utilization of invasive cardiac procedures in a UK ethnic population with unstable angina pectoris. *Int J Cardiol* 2001;77:275-80.
- xxx Bhopal R, Unwin N, White M, Yallop J, Walker L, Alberti KGMM, et al. Heterogeneity of coronary heart disease risk factors in Indian, Pakistani, Bangladeshi and European origin populations: cross sectional study. *BMJ* 1999;319:215-20.

- xxxvi Riste L, Khan F, Cruickshank K. High prevalence of type 2 diabetes in all ethnic groups including Europeans in a British inner city. *Diabetes Care* 2001;24:2-8.
- xxxvii McKeigue PM, Shah B, Marmot MG. Relation of central obesity and insulin resistance with high diabetes prevalence and cardiovascular risk in South Asians. *Lancet* 1991;337:382-6.
- xxxviii McKeigue PM, Ferrie JE, Pierpoint T, Marmot MG. Association of early onset coronary heart disease in South Asian men with glucose intolerance and hyperinsulinemia. *Circulation* 1993;87:152-61.
- xxxix Raji A, Seely EW, Arky RA, Simonson DC. Body fat distribution and insulin resistance in healthy Asian Indians and Caucasians. *J Clin Endocrinol Metab* 2001;86:5366-71.
- xl Kooner JS, Baliga RR, Wilding J, Crook D, Packard CJ, Banks LM, et al. Abdominal obesity, impaired non-esterified fatty acid suppression and insulin mediated glucose disposal are early metabolic abnormalities in families with premature myocardial infarction. *Arterioscler Thromb Vasc Biol* 1998;18:1021-6.
- xli Festa A, D'Agostino R, Howard G, Mykkänen L, Tracy RP, Haffner SM. Chronic subclinical inflammation as part of the insulin resistance syndrome. *Circulation* 2000;102:42-7.
- xlii Chambers JC, Shinichi E, Basset P, Karim Y, Simon GT, Gallimore R, et al. C-Reactive protein, insulin resistance, central obesity and coronary heart disease risk in Indian Asians from the United Kingdom compared to European whites. *Circulation* 2001;104:145-50.
- xliiii Thomas I, Gupta S, Sempos C, Cooper R. Serum lipids of Indian physicians living in U.S. compared to U.S.-born physicians. *Atherosclerosis* 1986;61:99-106.
- xliiiii Krishnaswami S, Prasad NK, Jose VJ. A study of lipid levels in Indian patients with coronary heart disease. *Int J Cardiol* 1989;24:337-45.

- xⁱ Kulkarni RK, Markovitz JH, Nanda NC, Segrest JP. Increased prevalence of smaller and dense LDL particles in Asian Indian. *Arterioscler Thromb Vasc Biol* 1999;19:2749-55.
- xⁱⁱ Bhatnagar D, Anand IS, Durrington PN, Patel DJ, Wander GS, Mackness M, et al. Coronary risk factors in people from the Indian Subcontinent living in West London and their siblings in India. *Lancet* 1995;345:405-9.
- xⁱⁱⁱ Chambers JC, Obeid OA, Refsum H, Ueland P, Hackett D, Hooper J, et al. Plasma homocysteine concentrations and the risk of coronary heart disease in UK Asian Indians and European men. *Lancet* 2000;355:523-7.
- xⁱⁱⁱⁱ Kain K, Catto AJ, Grant P. Impaired fibrinolysis and increased fibrinogen levels in South Asian subjects. *Atherosclerosis* 2001;156:457-61.
- x^{lv} Pais P, Pogue J, Gerstein H, Zachariah E, Savitha D, Jayprakash S, et al. Risk factors for acute myocardial infarction in Indians: a case-control study. *Lancet* 1996;348:358-63.
- x^{lvi} McGill HC, McMahan CA, Zieske AW, Malcom GT, Tracy RE, Strong JP. Effects of non-lipid risk factors on atherosclerosis in youth with a favorable lipoprotein profile. *Circulation* 2001;103:1546-50.
- x^{lvii} Gupta R. Coronary heart disease epidemiology in India: the past, present and future. In: Rao GHR, editor. *Coronary artery disease in South Asians*. 1st ed. New Delhi (India): Jaypee brothers medical publishers; 2001. p. 6-28.
- x^{lviii} Mohan V, Deepa R, Rani SS, Premalatha G. Prevalence of coronary heart 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.
- x^{lix} Pakistan Survey of Health and Living Conditions in the Elderly. Pakistan Medical Research Council. Islamabad (Pakistan), 2001, In Press.
- x^{lxi} Padmavati S, Gupta S. Blood pressure studies in rural and urban populations of Delhi. *Circulation* 1959;19:395-405.

- i Gupta R, Gupta S, Gupta VP, Parkash H. The prevalence and determinants of hypertension in the urban population of Jaipur in Western India. *J Hypertens* 1995;13:1193-200.
- ii National Health Survey of Pakistan 1990-94: Health profile of the people of Pakistan. Pakistan Medical Research Council. Islamabad (Pakistan), Network publication service; 1998.
- iii Fernando DJS, Siribaddana SH, De Silva DR, Perera SD. The prevalence of obesity and other coronary risk factors in a suburban Sri Lankan community. *Asia Pac J Clin Nutr* 1995;1:1-4.
- iiii Zaman MM, Rauf MA. Prevalence of hypertension in a Bangladesh adult population. *J Hum Hypertens* 1999;13:547-9.
- lv Statistical pocketbook of Bangladesh 1998. Bangladesh Bureau of Statistics, Statistics Division, Ministry of Planning, Government of the Peoples Republic of Bangladesh. Dhaka; June 1999.
- lv Matetzky S, Tani S, Kangavari S, Dimayuga P, Yano J, Xu H, et al. Smoking increases tissue factor expression in atherosclerotic plaques. Implications for plaque thrombogenicity. *Circulation* 2000;102:602-4.
- lvi Gupta R, Gupta VP. Urban and rural differences in coronary risk factors do not fully explain greater urban coronary heart disease prevalence. *J Assoc Phys Ind* 1997;45:683-6.
- lvii Mendis S. Cardiovascular research in Sri Lanka: review and bibliography, 1905-1998. Ministry of Health. Sri Lanka, 1998.
- lviii Zaman MM, Yoshiike N, Rouf MA, Syeed MH, Khan MR, Haque S, et al. Cardiovascular risk factors: distribution and prevalence in a rural population of Bangladesh. *J Cardiovasc Risk* 2001;8:103-8
- lix Squires WG Jr, Brandon TA, Zinkgraf S, Bonds D, Hartung GH, Murray T, et al. Hemodynamic effects of oral smokeless tobacco in dogs and young adults. *Prev Med* 1984;13:195-206.
- lx Bolinder G, Alfredsson L, Englund A, de Faire U. Smokeless tobacco use and increased cardiovascular mortality among Swedish construction workers. *Am J Public Health* 1994;84:399-404.

- lxi Executive summary of the third report of the National Cholesterol Education Programme (NCEP) expert panel on the Detection, Evaluation and Treatment of High Blood Cholesterol (Adult Treatment Panel 111). *JAMA* 2001;285:2486-97.
- lxii Stalmler J, Vaccaro O, Neaton JD, Wentworth D. Disease, other risk factors and 12-year cardiovascular mortality for men screened in the Multiple Risk Factor Intervention Trial. *Diabetes Care* 1993;16:434-44.
- lxiii Kannel WB, McGee DL. Diabetes and cardiovascular disease. The Framingham Study. *JAMA* 1979;241:2035-8.
- lxiv Manson JE, Colditz GA, Stampfer MJ, Willett WC, Krolewski AS, Rosner R, et al. A prospective study of maturity-onset diabetes mellitus and risk of coronary heart disease and stroke in women. *Arch Intern Med* 1991;151:1141-7.
- lxv Ramachandran A, Viswanathan M, Mahan V. Epidemiology of NIDDM in Indians. *J Assoc Phys Ind* 1993;41:1-4.
- lxvi Verma NP, Mehta SP, Madhu S, Mather HM, Keen H. Prevalence of known diabetes in an urban Indian environment: the Darya Ganj Diabetes Survey. *BMJ (Clin Res Ed)* 1986;293:423-4.
- lxvii Illanagasekera VLU, Nugegoda NB, Perera LS. Prevalence of diabetes mellitus and impaired glucose tolerance in a rural Sri Lankan community. *Cey Med J* 1993;348:358-63.
- lxviii Sayeed MA, Hussain MZ, Banu A, Rumi MA, Azad Khan AK. Prevalence of diabetes in a suburban population of Bangladesh. *Diabetes Res Clin Pract* 1997;34:149-55.
- lxix Hegele RA. Premature atherosclerosis associated with monogenic insulin resistance. *Circulation* 2001;103:2225-9
- lxx Hughes K, Yeo PP, Lun KC, Thai AC, Sothy SP, Wang KW, et al. Cardiovascular diseases in Chinese, Malays, and Indians in Singapore. II. Differences in risk factor levels. *J Epidemiol Community Health* 1990;44:29-35.

- lxxi Hughes K, Aw TC, Kuperan P, Choo M. Central Obesity, insulin resistance, syndrome X, lipoprotein (a) and cardiovascular risk in Indians, Malays and Chinese in Singapore. *J Epidemiol Community Health* 1997;51:394-9.
- lxxii Larsson B, Svardsudd K, Welin L, Wilhelmsen L, Bjorntorp P, Tibblin G. Abdominal adipose tissue distribution, obesity and the risk of cardiovascular disease and death: 13 year follow up of participants in the study of men born in 1913. *BMJ* 1984;288:1401-4.
- lxxiii Lapidus L, Bengtsson C, Larsson B, Pennert K, Rybo E, Sjostrom L. Distribution of adipose tissue and risk of cardiovascular disease and death: a twelve year follow up of participants in the population study of women in Gothenburg, Sweden. *BMJ* 1984;289:1257-61.
- lxxiv Reddy KS, Shah P, Shrivastava U, Prabhakaran D, Joshi M, Puri SK, et al. Coronary heart disease risk factors in an industrial population of north India. *Can J Cardiol* 1997;(13Suppl B):26B.
- lxxv Lemieux I, Pascot A, Couillard C, Lamarche B, Tchernof A, Alméras N, et al. Hypertriglyceridemic waist: A marker of the atherogenic metabolic triad (hyperinsulinemia; hyperapoprotein B; small dense LDL) in men. *Circulation* 2000;102:179-84.
- lxxvi Pi-Sunyer FX. Health implications of obesity. *Am J Clin Nutr* 1991;53:1595S-603S.
- lxxvii Mendis S. Comparative study of middle aged men in both rural and urban areas. *Proc KSM* 1996, 18: 64-94. Available from; URL; <http://cvdinfobase.ic.gc.ca/gcvi/default.htm> [last accessed 2001 Jun 26]
- lxxviii Shephard RJ, Balady GJ. Exercise as Cardiovascular Therapy. *Circulation* 1999;99:963-72.
- lxxix Kris-Etherton P, Eckel RH, Howard BV, Jeor SS, Bazzarre TL. Benefits of a Mediterranean-Style, National Cholesterol Education Programme/American Heart Association Step I dietary pattern on cardiovascular disease. *Circulation* 2001;103:1823-5.

- lxxx Gordon T, Castelli WP, Hjortland MC, Kannel WB, Dawber TR, et al. High density lipoprotein as a protective factor against coronary heart disease. The Framingham study. *Am J Med* 1977;62:707-14.
- lxxxi Gordon DJ, Knoke J, Probstfeld JL, Superko R, Tyroler HA, for the LRC Programme. High-density lipoprotein cholesterol and coronary heart disease in hypercholesterolemic men: the Lipid Research Clinics Coronary Primary Prevention Trial. *Circulation* 1986;74:1217-25.
- lxxxii Kannel WB, Neaton JD, Wentworth D, Thomas HE, Stamler J, Hulley SB, et al, for the MRFIT Research Group. Overall and coronary heart disease mortality rates in relation to major risk factors in 325,348 men screened for the MRFIT. Multiple Risk Factor Intervention Trial. *Am Heart J* 1986;112:825-36.
- ?
lxxxiii Bapat P. Ethnic variation of cord plasma apolipoprotein levels in relation to coronary risk level: a study in three ethnic groups of Singapore. *Acta Paediatrica* 1996; 85:1476-82
- lxxxiv Sandholzer C, Saha N, Kark JD, Rees A, Jaross W, Dieplinger H, et al. Apo(a) isoforms predict risk for coronary heart disease. A study in six populations. *Arterioscler Thromb* 1992;12:1214-26.
- lxxxv Mendis S, Ekanayake EM. Prevalence of coronary heart disease and cardiovascular risk factors in middle aged males in a defined population in central Sri Lanka. *Int J Cardiol* 1994;46:135-42.
- lxxxvi Ariyoa AA, Haan M, Tangen CM, Rutledge JC, Cushman M, Dobs A, et al. Depressive symptoms and risks of coronary heart disease and mortality in elderly Americans. *Circulation* 2000;102:1773-9.
- lxxxvii Willimas JE, Paton CC, Siegler IC, Eigenbrodt ML, Nieto FJ, Tyroler HA. Anger proneness predicts coronary heart disease risk: prospective analysis from the Atherosclerosis risk in communities study (ARIC). *Circulation* 2000;101:2034-9.
- lxxxviii Rozanski A, Blumenthal JA, Kaplan J. Impact of psychological factors on the pathogenesis of cardiovascular disease and implications for therapy. *Circulation* 1999;99:2192-217.
- lxxxix Denollet J, Vaes J, Brutsaert DL. Inadequate response to treatment in coronary heart disease: Adverse effects of Type D personality and

- younger age on 5-year prognosis and quality of life. *Circulation* 2000;102:630-5.
- ^{xc} Hemingway H, Whitty CJ, Shipley M, Stansfeld MS, Brunner E, Fuhrer R, et al. Psychological risk factors for coronary artery disease in white, South Asian and Afro Caribbean civil servants: the Whitehall 11 study. *Ethn Dis* 2001;11:391-400.
- ^{xcⁱ} Anand S, Yusuf S, Vuksan V, Devanesean S, Montague P, Kelemen L, et al. The Study of Health Assessment and Risk in Ethnic groups (SHARE): rationale and design. *Can J Cardiol* 1998;14:1349-57.
- ^{xcⁱⁱ} Zodpay SP, Raut SG. Coronary prone behavior pattern and risk of coronary heart disease: a case-control study. *Indian J Med Sci* 1998;52:348-51.
- ^{xcⁱⁱⁱ} King KB. Psychologic and social aspects of cardiovascular disease. *Ann Behav Med* 1997;19:264-70.
- ^{xc^{iv}} Barker DJ. In utero programming of cardiovascular disease. *Theriogenology* 2000;53:555-74.
- ^{xc^v} Godfrey DM, Barker DJ. Fetal nutrition and adult disease. *Am J Clin Nutr* 2000;71(5 suppl):1344S-52S.
- ^{xc^{vi}} Leeson CPM, Kattenhorn M, Morley R, Lucas A, Deanfield JE. Impact of low birth weight and cardiovascular risk factors on endothelial function in early adult life. *Circulation* 2001;103:1264-8.
- ^{xc^{vii}} Stein CE, Fall CH, Kumaran K, Osmond C, Cox V, Barker DJ. Fetal growth and coronary heart disease in South India. *Lancet* 1996;348:1269-73.
- ^{xc^{viii}} Rose G, Marmot MG. Social class and coronary heart disease. *Br Heart J* 1981;45:13-9.
- ^{xc^{ix}} Liu K, Cedres LB, Stamler J, Dyer A, Stamler R, Nanas S, et al. Relationship of education to major risk factors and death from coronary heart disease, cardiovascular diseases and all causes: Finding of three Chicago Epidemiological studies. *Circulation* 1982;66:1308-14.

- ^c Lynch J, Kaplan GA, Salonen R, Cohen RD, Salonen JT. Socioeconomic status and carotid atherosclerosis. *Circulation* 1995;92:1786-92.
- ^{ci} Gold MR, Franks P. The social origin of cardiovascular risk: an investigation in a rural community. *Int J Health Sev* 1990;20:405-16.
- ^{cii} Hoeymans N, Smit HA, Verkleij H, Krohout D. Cardiovascular risk factors in relation to educational level in 36,000 men and women in the Netherlands. *Eur Heart J* 1996;17:518-25.
- ^{ciii} Arnesen E, Forsdahl A. The Tromso Heart Study: coronary risk factors and their association with living conditions during childhood. *J Epidemiol and Community Health* 1985;39:210-4.
- ^{civ} Lynch JW, Kaplan GA, Salonen JT. Why do poor people behave poorly? Variations in adult health behaviours and psychosocial characteristics by stages of socio-economic life course. *Soc Sci Med* 1997;44:809-19.
- ^{cv} Obeid OA, Mannan N, Perry G, Iles RA, Boucher BJ. Homocystine and folate in healthy East London Bangladeshis. *Lancet* 1998;352:1829-30.
- ^{cvi} Abraham R, Brown MC, North WR, McFadyen IR. Diets of Asian pregnant women in Harrow: iron and vitamins. *Hum Nutr Appl Nutr* 1987;41:164-73.
- ^{cvii} Dawson DW, Waters HM. Malnutrition: folate and cobalamin deficiency. *Br J Biomed Sci* 1994;51:221-27.
- ^{cviii} Appel LJ, Miller ER 3rd, Jee SH, Stolzenberg-Soloman R, Lin PH, Erlinger T, et al. Effect of dietary patterns on serum homocysteine: results of a randomized controlled feeding study. *Circulation* 2000;102:852-7.
- ^{cix} Rupprecht HJ, Blankenberg S, Bickel C, Rippin G, Hafner G, Prellwitz W, Schlumberger W, Meyer J. Impact of viral and bacterial infectious burden on long-term prognosis in patients with coronary artery disease. *Circulation* 2001;104:25-31.

- cx Zhu J, Nieto FJ, Horne BD, Anderson JL, Muhlestein JB, Epstein SE. Prospective study of pathogen burden and risk of myocardial infarction or death. *Circulation* 2001;103:45-51.
- cxii Espinola-Klein C, Rupprecht HJ, Blankenberg S, Bickel C, Kopp H, Rippin G, et al. Impact of infectious burden on extent and long-term prognosis of atherosclerosis. *Circulation* 2002;105:15-21.
- cxiii Burian K, Kis Z, Virok D, Endresz V, Prohaszka Z, Duba J, et al. Independent and joint effects of antibodies to human heat-shock protein 60 and Chlamydia pneumoniae infection in the development of coronary atherosclerosis. *Circulation* 2001;103:1503-8.
- cxiiii Chambers JC, Shinichi E, Basset P, Karim Y, Simon GT, Gallimore R, et al. C-Reactive protein, insulin resistance, central obesity and coronary heart disease risk in Indian Asians from the United Kingdom compared to European whites. *Circulation* 2001;104:145-50.
- cxv Cook DJ, Mendall MA, Whincup PH, Carey IM, Ballam L, Morris JE, et al. C-Reactive protein concentrations in children: relationship to adiposity and other cardiovascular risk factors. *Atherosclerosis* 2000;149:139-50.
- cxvi Hegele RA. Premature atherosclerosis associated with monogenic insulin resistance. *Circulation* 2001;103:2225-9
- cxvii The Victoria Declaration on Heart Health 1992. Declaration of the Advisory Board of the 1st International Heart Health Conference. Victoria, British Columbia, 1992.
- cxviii Stampfer MJ, Hu FB, Manson JE, Rimm EB, Willet WC. Primary prevention of coronary heart disease in women through diet and lifestyle. *NEJM* 2000;343:16-22.
- cxix Puska P, Tuomilehto J, Nissinen A, Vartiainen E. editors. The North Karelia Project: 20 years of Results and Experiences. Helsinki (Finland). Helsinki, National Public Health Institute, 1995.
- cxix Fortmann SP, Flora JA, Winkleby MA, Schooler C, Taylor CB, Farquhar JW. Community intervention trials: reflections on the Stanford Five-City Project Experience. *Am J Epidemiol* 1995 Sep 15;142:576-86.

- ^{cxx} Zatonski WA, McMichael J, Powles JW. Ecological study of reasons for sharp decline in mortality from ischaemic heart disease in Poland since 1991. *BMJ* 1998;316:1047-51.
- ^{cxxi} Grundy SM, Balady GJ, Criqui MH, Fletcher G, Greenland P, Hiratzka LF, et al. Guide to the primary prevention of cardiovascular diseases: a statement for health care professionals from the task force on risk reduction. *Circulation* 1997;95:2329-31.
- ^{cxxii} Wood D, De Becker G, Faergamen O, Graham I, Mancia G, Pyörälä K, et al, on behalf of the task force. Summary of Recommendations of the task force of the European Society of Cardiology, European Atherosclerosis Society and European Society of Hypertension. *Prevention of Coronary Heart Disease in Clinical Practice*.
- ^{cxxiii} Murray CJC, 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: Harvard University press; 1996.
- ^{cxxiv} Balarajan R. Ethnic differences in mortality from ischaemic heart disease and cerebrovascular disease in England and Wales. *BMJ* 1991;302:560-4.
- ^{cxxv} Kaplan LA, Keil JE. Socioeconomic factors and cardiovascular disease: a review of literature. *Circulation* 1993;88:1973-98.
- ^{cxxvi} About Women Heart Disease and Stroke: an official publication of the American Heart Association. <http://www.americanheart.org/statistics/02about.html>
- ^{cxxvii} Office of the Population Census and Surveys, 1990. *Mortality and geography: a review in the mid 1980's*. The Registrar-Generals Decennial Supplement for England and Wales, Series DS no. 9. London. HMSO.
- ^{cxxviii} Reddy KS. Hypertension control in developing countries: generic issues. *J Hum Hypertens* 1996;10 Suppl 1:33S-8S.

- ^{cxxxix} Rodgers A, Lawes C, MacMahon S. Reducing the global burden of blood pressure related cardiovascular disease. *J Hypertens* 2000;18 Suppl 1:3S-6S.
- ^{cxxx} Yusuf S. Personal communication of the INTERHEART Data: A Global Study of Risk Factors in Acute Myocardial Infarction. McMaster University, sponsored by the World Health Organization, World Heart Federation and the International Clinical Epidemiology Network.
- ^{cxxxix} Cholesterol and coronary heart disease: screening and treatment. *Effective Health Care*. June 1998. In *Guidelines: summarizing clinical the guidelines for primary care*, Volume 10, 2000 Feb. NHS (UK) recommended guidelines.
- ^{cxxxii} Labarthe DR. Prevention of cardiovascular disease risk factors in the first place. *ProCOR* [serial online] 2000 Sep 20;99:167. Available from: URL: <http://www.procor.org>
- ^{cxxxiii} Strasser T. Reflections on cardiovascular disease. *Interdisc Sci Review* 1978;3:255-30.
- ^{cxxxiv} Pearce KA, Furberg CD, Psaty BM, Kirk J. Cost-minimization and the number needed to treat uncomplicated hypertension. *Am J Hypertens* 1998;11:618-29.
- ^{cxxxv} Philipp T, Anlauf M, Distler A, Holzgreve H, Michaelis J, Wellek S. Randomized, double blind, multicentre comparison of hydrochlorothiazide, atenolol, nitrendipine, enalapril in antihypertensive treatment; results of HANE study: HANE Trial Research Group. *BMJ* 1977;315:154-9.
- ^{cxxxvi} Secondary prevention of coronary heart disease. British Hyperlipidaemia Association. 1999 February. In *Guidelines: summarizing clinical guidelines for primary care*. Volume 10, 2000 Feb. NHS (UK) recommended guidelines.