Quality of life and medicine

Cardiovascular diseases

Preventive medicine review paper

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introduction

Quality of life or the *"well being"* of a population is an important concept in tow separated but overlapping plains: lifestyle and environmental factors and their effects on healthy people by increasing or decreasing the risks to develop a disease, and the quality of life of a patients already diagnosed with disease mainly how does their medical condition affect their life.
the identification of risk factors of the various form of heart diseases and the continuous effort to modify them in the healthy population and especially in people at higher risks, have a great impact on the ways health care systems today deal with patients with cardiovascular diseases and most importantly, the fact that there are many preventive measures that have an impact on developing the disease and modify its course. Cardiovascular disease is perhaps one of the most widespread health problems in recent history. Heart disease afflicts people around the world, chiefly living in modernized countries. A large amount of research public education, and clearly identifiable risk factors still does not prevent literally millions from being diagnosed with some form of cardiovascular disease each year. Likewise, the number of treatment interventions for heart disease are numerous as well, from pharmaceuticals to naturally derived medicines. True, despite all that we do know about this disease and all of its subtypes, much needs to be learned. However, the utilization of preventive medicines in those at risk for heart disease (in addition to lifestyle [diet, exercise] changes) can provide effective medical therapy, before much more drastic interventions are needed. The relations among life-style health behavior, social structure and support, health status and cardiovascular diseases will be explored in this review paper as well as the various efforts and possibilities of preventing the disease and modifying its development, progress, and outcomes.

Quality of life

many definitions of quality of life exist, of which I find the following one most reliable to describe the very close and important connections and interplay between quality of life and the health status of people, connections that will take us more time and researches to describe it all and to be useful in the overall concerns of many medical conditions that in the recent years are being central in the efforts of public health community.

The degree to which a person enjoys the important possibilities of his/her life. Possibilities result from the opportunities and limitations each person has in his/her life and reflect the interaction of personal and environmental factors. Enjoyment has two components: the experience of satisfaction and the

Possession or achievement of some characteristic, as illustrated by the expression: "She enjoys good health." Three major life domains are identified:

Being, Belonging, and Becoming. The conceptualization of Being, Belonging, and Becoming as the domains of quality of life were developed from the insights of various writers.

The ***Being*** domain includes the basic aspects of "who one is" and has three sub-domains. *Physical being* includes aspects of physical health, personal hygiene, nutrition, exercise, grooming, clothing, and physical appearance. *Psychological being* includes the person's psychological health and adjustment, cognitions, feelings, and evaluations concerning the self, and self-control. *Spiritual being* reflects personal values, personal standards of conduct, and spiritual beliefs which may or may not be associated with organized religions.

Belonging includes the person's fit with his/her environments and also has three sub-domains. *Physical Belonging* is defined as the connections the person has with his/her physical environments such as home, workplace, neighborhood, school and community. *Social Belonging* includes links with social environments and includes the sense of acceptance by intimate others, family, friends, co-workers, and neighborhood and community. *Community belonging* represents access to resources normally available to community members, such as adequate income, health and social services, employment, educational and recreational programs, and community activities.

Becoming refers to the purposeful activities carried out to achieve personal goals, hopes, and wishes. Practical Becoming describes day-to-day actions such as domestic activities, paid work, school or volunteer activities, and seeing to health or social needs. Leisure Becoming includes activities that promote relaxation and stress reduction. These include card games, neighborhood walks, and family visits, or longer duration activities such as vacations or holidays. Growth Becoming activities promote the improvement or maintenance of knowledge and skills.

The ***well-being*** or ***quality of life*** of a population is an important concern in economics and political science; there are many components to well-being. A large part is standard of living, the amount of money and access to goods and services that a person has; these numbers are fairly easily measured. Others like Freedom, happiness, art, environmental health, and innovation are far harder to measure and could be more important. This has created an inevitable imbalance as programs and policies are created to fit the easily available economic numbers while ignoring the other measures that are very difficult to plan for or assess. Debate on quality of life is millennia-old, with Aristotle giving it much thought in his *nicomachian ethics* and eventually settling on the notion of *eudaimonia*, a Greek term often translated as happiness, as central. The neologism **livability** (or **livability**), from the adjective *liv(e)able*, is an abstract noun now often applied to the built environment or a town or city, meaning its overall contribution to the quality of life of inhabitants. Understanding quality of life is today particularly important in health care, where monetary measures do

not readily apply. Decisions on what research or treatments to invest the most in are closely related to their effect of a patient's quality of life.

Measuring quality of life

The measures often used in the study of health care are **'quality-adjusted life years' (QALYs)** and the related **'disability-adjusted life years' (DALYs)**; both equal 1 for each year of full-health life, and less than 1 for various degrees of illness or disability. Thus the cost-effectiveness of a treatment can be assessed by the cost per QALY or DALY it produces; for example, a cancer treatment which costs $10,000 and on average gives the patient 2 extra years of full health costs $5000 per QALY. Assessing treatments in this way avoids the much greater problems associated with putting a monetary value on life, as required in other areas of economics; saying that a treatment *costs* $5000 per QALY (i.e. per year of life) does not say or assume anything about the monetary *value* of a year of life or about the real quality of that life. Whether it is worth living depends on the way of life or lifestyle. It may be questionable whether living two more years alone in a senior living facility is really adding value to life or whether it is depleting it, and disgracing human life and society itself. Another method of measuring quality of life is by subtracting the *"standard of living"*, according to the technical definition of the term. For example, people in rural areas and small towns are generally reluctant to move to cities, even if it would mean a substantial increase in their standard of living. One can thus see that the quality Of life of living in a rural area is of enough value to offset a higher standard of living. Similarly people must be paid more to accept jobs that will lower their quality of life, night jobs, ones with extensive travel all pay more and the difference in salaries can also give a measure of the value of quality of life. There is a growing field of research concerned with developing, evaluating and applying quality of life measures within health related research (e.g. within randomised controlled trials). Many of these focus on the measurement of health related quality of life (HRQoL), rather than a more global conceptualisation of quality of life. They also focus on measuring HRQoL from the perspective of the patient and thus take the form of self completed questionnaires. The International Society for Quality of Life was founded in response to this research and is a useful source of information.

Quality-adjusted life years

Quality-adjusted life years, or **QALYs**, are a measure of the benefit of a medical intervention. It is based on the number of years of life that would be added by the intervention. Each year in perfect health is assigned the value of 1.0 down to a value of 0 for death. If the extra years would not be lived in full health, for example if the patient would lose a limb, or be blind or be confined to a wheelchair, then the extra life-years are given a value between 0 and 1 to account for this. The "weight" values between 0 and 1 are usually determined by Time-trade-off (TTO), or the Standard gamble method. However, the weight

assigned to a particluar condition can vary greatly, depending on the population being surveyed. Those who do not suffer from the affliction in question will, on average, overestimate the detrimental effect on quality of life, while those who are afflicted have come to live with their condition. QALYs are controversial as the measurement is used to calculate the allocation of healthcare resources based upon a ratio of cost per QALY. As a result some people will not receive treatment as it is calculated that the benefit to their quality of life is not warranted by the cost.

Disability-adjusted life years

Disability-adjusted life years (DALY) is a measure for the overall "burden of disease." Originally developed by the World Health Organization, it is becoming increasingly common in the field of public health. It is designed to quantify the impact of premature death and disability on a population by combining them into a single measure. Traditionally, health liabilities were expressed using one measure: (expected or average number of) Years of Life Lost (YLL). This measure does not take the impact of disability into account, which can be expressed by: Years Lived with Disability (YLD). DALYs are calculated by taking the sum of these two components. In a formula: DALY = YLL + YLD. Looking at the burden of disease via DALYs can reveal surprising things about a population's health. For example, the 1990 WHO report indicated that 5 of the 10 leading causes of disability were psychiatric conditions. Psychiatric and neurologic conditions account for 28% of all years lived with disability, but only 1.4% of all deaths and 1.1% of years lost. Thus, psychiatric disorders, while generally not seen as a major epidemiological problem, are shown by consideration of disability years to have a huge impact on populations.

Health related quality of life (HRQL)

Quality of life is not related to medicine only by the epidemiological relations that try to link a disease to groups of people that are said to have higher risk to develop the disease, but also to the quality of life of those that already developed the disease and said to be patients. In the patients populations that receive the same treatment and medical interventions exists differences in the outcome and mainly in the quality of life after the treatment, both are extremely important for the overall health status of the patient. Many factors determine the variations in outcome such as sex, age, socioeconomic status, concomitant diseases and risk factors. Psychological factors and personality are also important.
Parallel to the diversity of definitions of QOL is an equal or greater diversity of Measurement tools used by different authors.
Increasingly disease-specific measures are being developed.
These measures are seen as necessary in order to capture the diversity of the effects of different conditions, as well as the typical age range of those most affected.

Most definitions of QOL in cardiac rehabilitation include reference to "social utility," frequently centered directly on return to work. This likely reflects the traditional focus of these programs on men for whom return to work may be a primary goal.
Similarly, Faden and German (1994) postulate that the meaning of QOL is age dependent, and that some changes such as increasing dependence may Have different values for different age groups.

Clinicians and policymakers are recognizing the importance of measuring health-related quality of life (HRQL) to inform patient management and policy decisions. Self- or interviewer-administered questionnaires can be used to measure cross-sectional differences in quality of life between patients at a point in time (discriminative instruments) or longitudinal changes in HRQL within patients during a period of time (evaluative instruments).
Both discriminative and evaluative instruments must be valid (really measuring what they are supposed to measure) and have a high ratio of signal to noise (reliability and responsiveness, respectively). Reliable discriminative instruments are able to reproducibly differentiate between persons. Responsive evaluative measures are able to detect important changes in HRQL during a period of time, even if those changes are small.

Health-related quality of life measures should also be interpretable—that is, clinicians and policymakers must be able to identify differences in scores that correspond to trivial, small, moderate, and large differences.
Two basic approaches to quality-of-life measurement are available: generic instruments that provide a summary of HRQL; and specific instruments that focus on problems associated with single disease states, patient groups, or areas of function. Generic instruments include health profiles and instruments that generate health utilities. The approaches are not mutually exclusive. Each approach has its strengths and weaknesses and may be suitable for different circumstances. Investigations in HRQL have led to instruments suitable for detecting minimally important effects in clinical trials, for measuring the health of populations, and for providing information for policy decisions.

Quality of Life (QOL) is an important outcome of medical care, and there is an increasing use of QOL measures in evaluations of treatment effectiveness. This is particularly evident in the field of rehabilitation of heart patients, where improving QOL is often given as the major goal of therapy (Day, 1993). In spite of general agreement concerning the importance of QOL as an outcome, the way in which this concept should be defined and measured is far from clear. *Chronic heart failure* is a significant health problem in the western world, and the incidence of newly diagnosed cases of heart failure continues to increase.

HRQOL in patients with heart disease

According to the American Heart Association, heart failure affects more than 4.9 million persons in the United States, and 550000 new cases occur annually. Heart failure has a high mortality rate, with a 12-month rate of approximately 15% and a 5-year rate of 50%. In addition, a considerable financial burden results from the high rates of hospitalization, readmission, visits to physicians' offices, and complicated treatment regimens. These patients are often admitted to critical care units for stabilization after episodes of acute decompensation. *Health-related quality of life (HRQL)* is greatly diminished among patients with heart failure. Patients experience a variety of uncomfortable signs and symptoms and reduced physical, psychological, and social function. Importantly, *HRQL* is a significant predictor of hospitalization and mortality among chronically ill patients with heart failure.

The incidence of heart failure increases with older age, and the risk factors for heart failure may be different for women and men. Additionally, women and men may respond differently to the impact of heart failure. However, the relationships of age and sex of patients to HRQL and to changes in HRQL over time are not clear. Findings from previous studies of the relationship between age and HRQL have been inconsistent, with a suggestion that older patients do not necessarily experience poorer HRQL. Older age in patients with heart failure has been associated with an increase in general life satisfaction, better overall life satisfaction and HRQL, and worse emotional functioning, although Westlake et al did not find that age was a significant correlate of physical or emotional components of HRQL.

Investigators have also examined the relationship between sex of the patient and quality of life. Minimal differences in HRQL between women and men were reported in samples of patients (including women but not the same number) On the other hand, Riedinger et al reported that women had significantly worse general health and physical function than did men once age, left ventricular ejection fraction, and New York Heart Association (NYHA) class had been controlled for, but they found no differences in emotions between women and men as measured by the Profile of Mood States. These studies suggest that sample sizes may contribute to the inconsistent findings about differences in HRQL between women and men. Small sample sizes may limit the likelihood of findings being statistically significant. In a study in which NYHA class, age, and ejection fraction were matched in a sample of 640 patients with heart failure (50% women), Riegel et al found that women had worse emotional HRQL at baseline, both women and men had significantly improved HRQL during the 3-month study period, and women and men did not differ significantly after 3 months. However, in another study, women had worse physical functioning at baseline and less

improvement than men in physical function during a 1-year study period with no differences between the sexes in emotional HRQL as measured by the SF-36 Health Survey during the study period. In a study of a sample of 227 patients with heart failure, small changes in social support occurred that were nonetheless predictive of HRQL over 12 months. However, age was not related to changes in HRQL, and no difference was found in HRQL between women and men. Information on the relationships of patients' age and sex and the interactions of those 2 factors to HRQL and to changes in HRQL over time is important. Such information can be incorporated into critical care nurses' assessments, so that realistic goals can be established and appropriate interventions designed for specific, demographic populations. Previous studies provide some information, although results of those studies have been inconsistent. More information would help optimize individualized, effective interventions to improve HRQL among patients with heart failure and primarily among patients in the groups with poorest HRQL scores. Therefore, the specific aims of many study were to examine the differences in HRQL at baseline and after 26 weeks among 4 groups of patients with heart failure, that is, men less than 65 years old, men 65 years and older, women less than 65 years old, and women 65 years and older, and to evaluate interactions of age and sex with the changes in HRQL during 6 months, after controlling for the influence of race, marital status, living status, perceived income, educational level, baseline NYHA class, mental status scores, and baseline HRQL.

Measurement

There are three reasons we offer treatment to our patients. We believe our interventions increase longevity, prevent future morbidity, or make patients feel better. The first two of these three endpoints are relatively easy to measure. At least in part because of difficulty in measurement, clinicians have for many years been ready to substitute physiological or laboratory tests for the direct measurement of the third. In the last 20 years, however, clinicians have recognized the importance of direct measurement of how people are feeling, and how they are able to function in daily activities. Investigators have developed increasingly sophisticated methods of making these measurements. Since, as clinicians, we are most interested in aspects of life quality directly related to health rather than issues such as finances, or the quality of the environment, we frequently refer to measurements of how people are feeling as health-related quality of life (*HRQL*). Investigators measure HRQL using questionnaires that typically include questions about how patients are feeling or what they are experiencing associated with *response options* such as yes-no, or seven-point scales, or visual analogue scales. Investigators aggregate responses to these questions into *domains* or *dimensions* (such as physical or emotional function) that yield an overall score. Controversy exists concerning the boundaries of HRQL, and the extent to which individual patient's values must be included in its measurement. Is it sufficient to know that patients with chronic obstructive lung

disease in general value being able to climb stairs without getting short of breath, or does one need to establish that the individual patient values climbing stairs without dyspnea? Further controversy exists about how the relative values of items and domains need to be established, and how these values should be determined. Is it enough to know that both dyspnea and fatigue are important to people with lung disease, or does one need to establish their relative importance? If establishing their relative importance is necessary, which of the many available approaches should one use?

cardiovascular diseases

Extensive clinical and statistical studies have identified several factors that increase the risk of coronary heart disease and heart attack. Major risks factors are those that research has shown significantly increase the risk of cardiovascular disease. Other factors are associated with increased risk of cardiovascular disease, but their significance and prevalence haven't yet been precisely determined. They're called contributing risk factors. The American Heart Association has identified several risk factors. Some of them can be modified, treated or controlled, and some can't. The more risk factors a patient has, the greater his/her chance of developing coronary heart disease. Also, the greater the level of each risk factor, the greater the risk. For example, a person with total cholesterol of 300 mg/dL has a greater risk than someone with total cholesterol of 245 mg/dL, even though everyone with total cholesterol greater than 240 mg/dL is considered high-risk.

Heart disease and stroke are the most common cardiovascular diseases. They are the first and third leading causes of death for both men and women in the western world, accounting for nearly 40% of all annual deaths. More than 910,000 Americans die of cardiovascular diseases each year, which is *1 death every 35 seconds.* Although these largely preventable conditions are more common among people aged 65 or older, the number of sudden deaths from heart disease among people aged 15–34 has increased. In addition, more than 70 million Americans currently live with a cardiovascular disease. Coronary heart disease is a leading cause of premature, permanent disability in the U.S. and western world workforce. Stroke alone accounts for disability among about 1 million Americans. More than 6 million hospitalizations each year are because of cardiovascular diseases. The economic impact of cardiovascular diseases on our nation's health care system continues to grow as the population ages. The cost of heart disease and stroke in the United States is projected to be $403 billion in 2006, including health care expenditures and lost productivity from death and disability.

Cardiovascular disease related to class and lifestyle

Those with less education run twice as great a risk of dying of cardiovascular disease as white-collar workers in higher positions.

Established lifestyle patterns – from as far back as childhood – are linked to poor health and mortality in later life. This has been shown by a study of almost 50,000 Swedish men carried out at the National Institute for Working Life. The group's socio-economic status and other social factors were studied for the first time when they were boys aged 9–11, again when they enrolled for national service aged 18–20 and finally in 1990 when they were aged 39–41. Between 1990 and 2000 their health and mortality were followed up. Cardiovascular disease is a class issue – the lower the social and socio-economic position, the greater the risk. Factors such has having grown up in crowded conditions and in a low-income family were more common among blue-collar workers than white-collar workers in higher positions. At the age of 18–20 the blue-collar workers also demonstrated risk behaviours in terms of alcohol consumption, smoking and being overweight to a higher extent than the white-collar workers. The value of a family history of coronary heart disease (CHD) is increased when the age, sex, number of relatives, and age at onset of disease are incorporated in a quantitative family risk score. *Medical and lifestyle risk factors that aggregate in families include dyslipidemia, hypertension, obesity, hyperfibrinogenemia, diabetes mellitus, smoking habits, eating patterns, alcohol consumption, physical activity, and socioeconomic status.* Advances in detecting and understanding interactions between genetic susceptibility and modifiable risk factors should lead to improvements in prevention and treatment. However, working with families can be difficult. In the western world, families are usually small, are often widely dispersed, and may not be intact. Family histories may be unknown, affected relatives may be dead, and secular trends mask similarities among generations. Many exposures occur outside the home, and families change over time. Ethical, legal, and social issues arise when dealing with families. Nevertheless, opportunities are missed when research, clinical practice, and prevention focus on individual patients. Greater emphasis on families is needed to reduce the burden of CHD.

non-modifiable risk factors

Increasing Age: About 80 percent of people who die from coronary heart disease are age 65 or older. The prevalence of having one or more CVD risk factors increased with increasing age. The prevalence of having [greater than or equal to]2 risk factors was highest among respondents aged [greater than or equal to]65 years. Age is the strongest risk factor for the development of CAD. Elderly persons still experience higher mortality and morbidity rates from CAD. Complication rates of multiple therapeutic interventions tend to be higher; however, the magnitude of benefit from the same interventions is greater because these patients form the high-risk subgroup.

Sex: Men traditionally have a higher prevalence of CAD. Women, however, follow men by 10 years, especially after menopause. Nevertheless, the value of

estrogen supplementation has been discredited by the Heart and Estrogen/Progestin Replacement Study (HERS) (Schrott, 1997; Vittinghoff, 2003). The presence of diabetes eliminates the protection associated with female sex.

Even in women, the most common cause of death is CAD, which accounts for more deaths than those related to breast and uterine diseases combined. Women with AMI present later than average, are less often subjected to invasive strategies, and experience greater overall mortality. Similar statistics can also be cited for the presentation and treatment of patients with stable CAD.

Race (and genetics): The incidence, prevalence, and manifestations of CAD vary significantly with race, as does the response to therapy. African Americans appear to have higher morbidity and mortality rates, even when corrected for educational and socioeconomic status. The risk-factor burden experienced by African Americans differs from that of whites. The prevalence of hypertension, obesity, dysmetabolic syndrome(syndrome x), and lack of physical activity are much higher, whereas the prevalence of hypercholesterolemia is lower. African Americans with AMI present later than average, are less often subjected to invasive strategies, and experience greater overall mortality. Similar statistics can also be cited for presentation and treatment of patients with stable CAD.

- Asian Indians exhibit a 2- to 3-fold higher prevalence of CAD than whites in the United States. They have greater prevalence of hypoalphalipoproteinemia, high lipoprotein(a) levels, and diabetes.
- People in Mediterranean areas have a lower prevalence of CAD.

Major risk factors that can be modified, treated or controlled by changing patient's lifestyle or by taking medicine.

Cigarette Smoking and Cardiovascular Diseases

Cigarette smoking is the most important preventable cause of premature death in the western world. Cigarette smokers have a higher risk of developing a number of chronic disorders. These include fatty buildups in arteries, several types of cancer and chronic obstructive pulmonary disease. Atherosclerosis is a chief contributor to the high number of deaths from smoking. Many studies detail the evidence that cigarette smoking is a major cause of coronary heart disease, which leads to heart attack. Cigarette and tobacco smoke, high blood cholesterol, high blood pressure, physical inactivity, obesity and diabetes are the six major independent risk factors for coronary heart disease that you can modify or control. Cigarette smoking is so widespread and significant as a risk factor that the Surgeon General has called it *"the leading preventable cause of disease and deaths in the United States."* Cigarette smoking increases the risk of coronary

heart disease by itself. When it acts with other factors, it greatly increases risk.

Smoking increases blood pressure, decreases exercise tolerance and increases the tendency for blood to clot. Smoking also increases the risk of recurrent coronary heart disease after bypass surgery. Cigarette smoking is the most important risk factor for young men and women. It produces a greater relative risk in persons under age 50 than in those over 50. Women who smoke and use oral contraceptives greatly increase their risk of coronary heart disease and stroke compared with nonsmoking women who use oral contraceptives. Smoking decreases HDL (good) cholesterol. Cigarette smoking combined with a family history of heart disease also seems to greatly increase the risk. Studies show that cigarette smoking is an important risk factor for stroke. Inhaling cigarette smoke produces several effects that damage the cerebrovascular system. Women who take oral contraceptives and smoke increase their risk of stroke many times. Smoking also creates a higher risk for peripheral arterial disease and aortic aneurysm.
People who smoke cigars or pipes seem to have a higher risk of death from coronary heart disease (and possibly stroke), but their risk isn't as great as that of cigarette smokers. This is probably because they're less likely to inhale the smoke.Currently, there's very little scientific information on cigar and pipe smoking and cardiovascular disease, especially among young men, who represent the vast majority of cigar users. The link between seconhand smoke (also called environmental tobacco smoke) and disease is well known, and the connection to cardiovascular-related disability and death is also clear. About 37,000 to 40,000 people die from heart and blood vessel disease caused by other people's smoke each year. Of these, about 35,000 nonsmokers die from coronary heart disease, which includes heart attack.

Hypertension

High blood pressure — High blood pressure increases the heart's workload, causing the heart to thicken and become stiffer. It also increases your risk of stroke, heart attack, kidney failure and congestive heart failure. When high blood pressure exists with obesity, smoking, high blood cholesterol levels or diabetes, the risk of heart attack or stroke increases several times.

Background: Uncontrolled and prolonged elevation of blood pressure (BP) can lead to a variety of changes in the myocardial structure, coronary vasculature, and conduction system of the heart. These changes can lead to the development of left ventricular hypertrophy (LVH), coronary artery disease, various conduction system diseases, and systolic and diastolic dysfunction of the myocardium, which manifest clinically as angina or myocardial infarction, cardiac arrhythmias (especially atrial fibrillation), and congestive heart failure (CHF). Thus, hypertensive heart disease is a term applied generally to heart diseases, such as LVH, coronary artery disease, cardiac arrhythmias, and CHF, caused by direct or

indirect effects of elevated BP. Although these diseases generally develop in response to chronically elevated BP, marked and acute elevation of BP can also lead to accentuation of an underlying predisposition to any of the symptoms traditionally associated with chronic hypertension.

Compared with Whites, African Americans report higher rates of hypertension, diabetes, and arthritis, while Hispanics report higher rates of hypertension and diabetes and a lower rate of heart conditions. Accounting for differences in education, income, and wealth had little effect on these prevalence differences. In general, among those with cardiovascular diseases, African Americans and Hispanics reported worse function than Whites. This disadvantage was eliminated in every case by controlling for socioeconomic status. While socioeconomic status, including wealth, accounts for much of the difference in functional status associated with chronic cardiovascular diseases. It plays a relatively small role in explaining differences in the prevalence of chronic disease, possibly reflecting different causal pathways.

Pathophysiology: The pathophysiology of hypertensive heart disease is a complex interplay of various hemodynamic, structural, neuroendocrine, cellular, and molecular factors. On one hand, these factors play integral roles in the development of hypertension and its complications; on the other hand, elevated BP itself can modulate these factors. Elevated BP leads to adverse changes in cardiac structure and function in 2 ways: directly by increased afterload and indirectly by associated neurohormonal and vascular changes. Elevated 24-hour ambulatory BP and nocturnal BP have been demonstrated to be more closely related to various cardiac pathologies, especially in African Americans.

Left ventricular hypertrophy

Of patients with hypertension, 15-20% develop LVH. The risk of LVH is increased 2-fold by associated obesity. The prevalence of LVH based on ECG findings, which are not a sensitive marker at the time of diagnosis of hypertension, is variable. There is a direct relationship between the level and duration of elevated BP and LVH. LVH, defined as an increase in the mass of the left ventricle (LV), is caused by the response of myocytes to various stimuli accompanying elevated BP. Myocyte hypertrophy can occur as a compensatory response to increased afterload. Mechanical and neurohormonal stimuli accompanying hypertension can lead to activation of myocardial cell growth, gene expression (Some of the genes are given expression primarily in fetal cardiomyocytes.), and, thus, LVH. In addition, activation of the renin-angiotensin system, through the action of angiotensin II on angiotensin I receptors, leads to growth of interstitium and cell matrix components. Thus, the development of LVH is characterized by myocyte hypertrophy and by an imbalance between the myocytes and the interstitium of the myocardial skeletal structure. While the development of LVH initially plays a protective role in response to increased wall stress to maintain adequate cardiac output, later it leads to the development of diastolic and, ultimately, systolic

myocardial dysfunction.

Left atrial abnormalities

Frequently underappreciated, structural and functional changes of the left atrium (LA) are very common in patients with hypertension. The increased afterload imposed on the LA by the elevated LV end-diastolic pressure secondary to increased BP leads to impairment of the LA and LA appendage function plus increased LA size and thickness. Increased LA size accompanying hypertension in the absence of valvular heart disease or systolic dysfunction usually implies chronicity of hypertension and may correlate with the severity of LV diastolic dysfunction. In addition to these structural changes, these patients are predisposed to atrial fibrillation. Atrial fibrillation, with loss of atrial contribution in the presence of diastolic dysfunction, may precipitate overt heart failure.

Valvular disease

Although valvular disease does not cause hypertensive heart disease, chronic and severe hypertension can cause aortic root dilatation, leading to significant aortic insufficiency. Some degree of hemodynamically insignificant aortic insufficiency is often found in patients with uncontrolled hypertension. An acute rise in BP may accentuate the degree of aortic insufficiency, with return to baseline when BP is better controlled. In addition to causing aortic regurgitation, hypertension is also thought to accelerate the process of aortic sclerosis and cause mitral regurgitation.

Heart failure

Heart failure is a common complication of chronically elevated BP. Hypertension as a cause of CHF is frequently underrecognized, partly because at the time heart failure develops, the dysfunctioning LV is unable to generate the high BP, thus obscuring the etiology of the heart failure. The prevalence of asymptomatic diastolic dysfunction in patients with hypertension and without LVH may be as high as 33%. Chronically elevated afterload and resulting LVH can adversely affect both the active early relaxation phase and late compliance phase of ventricular diastole. Diastolic dysfunction is common in persons with hypertension. It is usually, but not invariably, accompanied by LVH. In addition to elevated afterload, other factors that may contribute to the development of diastolic dysfunction include coexistent coronary artery disease, aging, systolic dysfunction, and structural abnormalities such as fibrosis and LVH. Asymptomatic systolic dysfunction usually follows. Later in the course of disease,the LVH fails to compensate by increasing cardiac output in the face of elevated BP and the left ventricular cavity begins to dilate to maintain cardiac output. As the disease enters the end stage, LV systolic function decreases further. This leads to further increases in activation of the neurohormonal and renin-angiotensin systems, leading to increases in salt and water retention and increased peripheral vasoconstriction, eventually overwhelming the already

compromised LV and progressing to the stage of symptomatic systolic dysfunction. Apoptosis, or programmed cell death, stimulated by myocyte hypertrophy and the imbalance between its stimulants and inhibitors, is considered to play an important part in the transition from compensated to decompensated stage. The patient may become symptomatic during the asymptomatic stages of the LV systolic or diastolic dysfunction, owing to changes in afterload conditions or to the presence of other insults to the myocardium (eg, ischemia, infarction). A sudden increase in BP can lead to acute pulmonary edema without necessarily changing the LV ejection fraction. Generally, development of asymptomatic or symptomatic LV dilatation or dysfunction heralds rapid deterioration in clinical status and markedly increased risk of death. In addition to LV dysfunction, right ventricular thickening and diastolic dysfunction also develop as results of septal thickening and LV dysfunction.

Myocardial ischemia

Patients with angina have a high prevalence of hypertension. Hypertension is an established risk factor for the development of coronary artery disease, almost doubling the risk. The development of ischemia in patients with hypertension is multifactorial. Importantly, in patients with hypertension, angina can occur in the absence of epicardial coronary artery disease. The reason is 2-fold. Increased afterload secondary to hypertension leads to an increase in left ventricular wall tension and transmural pressure, compromising coronary blood flow during diastole. In addition, the microvasculature, beyond the epicardial coronary arteries, has been shown to be dysfunctional in patients with hypertension and it may be unable to compensate for increased metabolic and oxygen demand. The development and progression of arteriosclerosis, the hallmark of coronary artery disease, is exacerbated in arteries subjected to chronically elevated BP. Shear stress associated with hypertension and the resulting endothelial dysfunction causes impairment in the synthesis and release of the potent vasodilator nitric oxide. A decreased nitric oxide level promotes the development and acceleration of arteriosclerosis and plaque formation.Morphologic features of the plaque are identical to those observed in patients without hypertension.

Cardiac arrhythmias

Cardiac arrhythmias commonly observed in patients with hypertension include atrial fibrillation, premature ventricular contractions, and ventricular tachycardia. The risk of sudden cardiac death is increased. Various mechanisms thought to play a part in the pathogenesis of arrhythmias include altered cellular structure and metabolism, inhomogeneity of the myocardium, poor perfusion, myocardial fibrosis, and fluctuation in afterload. All of these may lead to an increased risk of ventricular tachyarrhythmias. Atrial fibrillation (paroxysmal, chronic recurrent, or chronic persistent) is observed frequently in patients with hypertension. In fact, elevated BP is the most common cause of atrial fibrillation in the Western hemisphere. In one study, nearly 50% of patients with atrial fibrillation had

hypertension. Although the exact etiology is not known, left atrial structural abnormalities, associated coronary artery disease, and LVH have been suggested as possible contributing factors. The development of atrial fibrillation can cause decompensation of systolic and, more importantly, diastolic Dysfunction, owing to loss of atrial kick, and it also increases the risk of thromboembolic complications, most notably stroke. Premature ventricular contractions, ventricular arrhythmias, and sudden cardiac death are observed more often in patients with LVH than in those without LVH. The etiology of these arrhythmias is thought to be concomitant coronary artery disease and myocardial fibrosis.

Frequency: The exact frequency is unknown. The rate of LVH based on ECG findings is 2.9% for men and 1.5% for women. The rate of LVH based on echocardiography findings is 15-20%. Of patients without LVH, 33% have evidence of asymptomatic LV diastolic dysfunction. Hypertension accounts for 10% of cases of CHF and, in the elderly population, as many as 68%. Some community-based studies have demonstrated that hypertension may contribute to the development of heart failure in as many as 50-60% of patients. In patients with hypertension, the risk of heart failure is increased by 2-fold in men and by 3-fold in women.

Mortality/Morbidity: Mortality and morbidity rates from hypertensive heart disease are higher than those of the general population and depend on the specific cardiac pathology. Data suggest that increases in mortality and morbidity rates are related more to the pulse pressure than the absolute systolic or diastolic BP levels, but all are important. The 5-year mortality rate for patients with heart failure due to systolic dysfunction approaches 20%, while the 2-year mortality rate in patients with NYHA class IV classification is as high as 50%. Mortality rates have decreased with use of ACE inhibitors and beta-blockers, which improve LV function.

cholesterol

Cholesterol is a steroid lipid, found in the cell membranes of all body tissues, and transported in the blood plasma, of all animals. Most cholesterol is produced internally, not dietary in origin. It is present in higher concentrations in tissues which either produce more or have more densely packed membranes; for example the liver, spinal cord, brain and atheroma. Cholesterol plays a central role in many biochemical processes, but is best known for the association of cardiovascular disease with various lipoprotein cholesterol transport patterns in the blood. Although cholesterol serves many important functions in the body, too much cholesterol in the blood can be dangerous. When blood cholesterol reaches high levels, it can build up on artery walls, increasing the risk of blood clots, heart attack and stroke. The bloodstream transports cholesterol throughout the body by special carriers called lipoproteins. The two major lipoproteins are low density lipoproteins (LDL) and high density lipoproteins (HDL). LDL is most

often referred to as the "bad" cholesterol whereas HDL is knows the "good" cholesterol. In healthy individuals the low-density lipoprotein (LDL) particles are large and relatively few in number. Conversely, large numbers of small low-density lipoprotein (LDL) particles are strongly associated with promoting atheromatous disease within the arteries. Other contributing factors are Increasing age: Being male greater than 45 years old or being female greatethan 55 years old (or having premature menopause without estrogen replacement therapy) and Heredity: A family history of premature heart disease (that is, having a father or other first-degree male relative who had a heart attack or died suddenly before the age of 55 years or having a mother or other first-degree female relative who had a heart attack or died suddenly before the age of 65 years). There is a graded increase in diabetes, hypertension and high serum cholesterol with increasing body weight in nearly all gender, racial and socioeconomic groups. Among the obese individuals, the prevalence of hypertension was higher in black subjects and the prevalence of diabetes, hypertension and heart disease was higher in individuals with lower education compared to their counterparts. The odds of having diabetes, hypertension, heart disease and high serum cholesterol increased with increasing body weight after adjusting for age, gender, race, income, education and smoking.

obesity

Obesity is a condition in which the natural energy reserve of a person, which is stored in fat, is expanded far beyond usual levels to the point where it is believed to pose a health risk. Obesity is a concept that is being continually redefined. In humans, the current measurement of obesity is the body mass index (BMI).

A person with a BMI over 25 kg/m2 is considered overweight; a BMI over 30kg/m2 is considered obese. The American Institute for Cancer Research considers a BMI between 18.5 and 25 to be an ideal target for a healthy individual (although several sources consider a person with a BMI of less than 20 to be underweight). The BMI was created in the 19th century by the Belgian statistician Adolphe Quetelet, and remained largely intact until June 1998 when the BMI was revised downward. This had the remarkable effect of changing some people's status from "ideal" weight to "overweight" in one day!

Like the weight-to-height table, BMI does not show the difference between excess fat and muscle. BMI, however, is closely associated with measures of body fat. It also predicts the development of health problems related to excess weight. For these reasons, BMI is widely used by health care providers.

Genetic, environmental, psychological, and other factors may all play a role in the development of obesity. Obesity tends to run in families, suggesting a genetic cause. But genes do not destine people to a lifetime of obesity. Although we cannot change your genetic makeup, you can change your eating habits and levels of activity

Environmental factors strongly influence obesity. This includes lifestyle behaviors such as what you eat and your level of physical activity. Most Americans do not get enough physical activity. Many also tend to eat high-fat foods, and put taste and convenience ahead of nutrition. Psychological factors may also influence eating habits. Many people eat in response to negative emotions such as boredom, sadness, or anger. Up to 10 percent of people who are mildly obese -- and even more who are severly obese -- have binge eating disorder. Those with the most severe binge eating problems are also likely to have symptoms of depression and low self-esteem.

Some illnesses also can lead to obesity, including hypothyroidism, Cushing's syndrome, depression, and certain neurological problems that can lead to overeating. Also, drugs such as steroids and some antidepressants may cause weight gain.

Although there is no definitive explanation for the recent epidemic of obesity, the evolutionary hypothesis comes closest to providing some understanding of this phenomenon. In times when food was scarce, the ability to take advantage of rare periods of abundance and use such abundance by storing energy efficiently was undoubtedly an evolutionary advantage. This is precisely the opposite of what is required in a sedentary society, where high-energy food is available in abundant quantities in the context of decreased exercise. Although many people May have a genetic propensity towards obesity, it is only with the reduction in physical activity and a move towards high-calorie diets of modern society that it has become widespread. Significant proportions (up to 30%) of the population in wealthy countries are now obese, and seen to be at risk of ill health.

Eating disorders can lead to obesity, especially binge eating disorder (BED). As the name indicates, patients with this disorder are prone to overeat, often in binges. A proposed mechanism is that the eating serves to reduce anxiety, and some parallels with substance abuse can be drawn. An important additional factor is that BED patients often lack the ability to recognize hunger and satisfaction, something that is normally learnt in childhood. Learning theory suggests that early childhood conceptions may lead to an association between food and a calm mental state.

Obesity is not just a cosmetic problem. It's a health hazard. Someone who is 40% overweight is twice as likely to die prematurely than an average-weight person. This is because obesity has been linked to several serious medical conditions including: insulin resistance, heart disease and stroke, high blood pressure, type 2 (adult-onset) diabetes, cancer, gallbladder disease and gallstones, osteoarthritis, gout, breathing problems, such as sleep apnea (when a person stops breathing for a short time during sleep) and asthma. All has a great impact and consequences on the overall quality of life of a patient and the worse thing is that they greatly influence the disease progress, the outcome of the medical therapy and limits the intervention and preventive measures that

otherwise would be undertaken. All in the end culminate to the undesirable inability of the patient to rehabilitate and to improve from the heart disease.

Heart disease and stroke: The Nurses Health Study found that the risk of developing coronary artery disease increased 3 to 4 times in women who had a BMI greater than 29. A Finnish study showed that for every one kilogram (2.2 pounds) increase in body weight, the risk of death from coronary artery disease increased by one percent. In patients who have already had a heart attack, obesity is associated with an increased likelihood of a second heart attack. Heart disease and stroke are the leading causes of death and disability. Overweight people are more likely to have high blood pressure, a major risk factor for heart disease and stroke, than people who are not overweight. Very high blood levels of cholesterol can also lead to heart disease and often are linked to being overweight. Being overweight also contributes to angina (chest pain caused by decreased oxygen to the heart) and sudden death from heart disease or stroke without any signs or symptoms.

Certain groups are affected more than others:

Among women, overweight and obesity are more prevalent in racial and ethnic minorities than in non-Hispanic white women. Among men, overweight and obesity are more prevalent in Mexican-Americans than in non-Hispanic whites or blacks. More non-Hispanic black women are overweight or obese than non-Hispanic black men. More non-Hispanic white men are overweight or obese than non-Hispanic white women. Women of lower socioeconomic status are approximately 50% more likely to be obese than those of higher socioeconomic status.

Diabetes mellitus

Diabetes seriously increases the risk of developing cardiovascular disease. Even when glucose levels are under control, diabetes increases the risk of heart disease and stroke, but the risks are even greater if blood sugar is not well controlled. About three-quarters of people with diabetes die of some form of heart or blood vessel disease. For patients with diabetes, it's extremely important to work with healthcare provider to manage it and control any other risk factors.

This statement examines the cardiovascular complications of diabetes mellitus and considers opportunities for their prevention. These complications include coronary heart disease (CHD), stroke, peripheral arterial disease, and cardiomyopathy. Because of the aging of the population and an increasing prevalence of obesity and sedentary life habits in the western world, the prevalence of diabetes is increasing. Thus, diabetes must take its place alongside the other major risk factors as important causes of cardiovascular disease (CVD). In fact, from the point of view of cardiovascular medicine, it may be appropriate to say, "diabetes *is* a cardiovascular disease."

At least 10.3 million Americans carry a diagnosis of diabetes mellitus. Around 5.4 million are estimated to have undiagnosed diabetes. Approximately 90% of patients with diabetes have the type 2 variety. The onset of type 2 diabetes usually precedes clinical diagnosis by several years. An increasing prevalence of type 2 diabetes cannot be divorced from the rising prevalence of obesity and physical inactivity in our society. An estimated 97 million adults in the United States are overweight or obese. body fat and physical inactivity predispose to type 2 diabetes. Several ethnic groups are particularly susceptible to type 2 diabetes: Hispanics, blacks, Native Americans, and Asians (especially South Asians). The growing ethnic diversity, including these groups, contributes to the increasing prevalence of type 2 diabetes in the United States.

A large body of epidemiological and pathological data documents that diabetes is an independent risk factor for CVD in both men and women. Women with diabetes seem to lose most of their inherent protection against developing CVD. CVDs are listed as the cause of death in 65% of persons with diabetes. Diabetes acts as an independent risk factor for several forms of CVD. To make matters worse, when patients with diabetes develop clinical CVD, they sustain a worse prognosis for survival than do CVD patients without diabetes.

Prospective studies indicate that all of the major cardiovascular risk factors—cigarette smoking, hypertension, and high serum cholesterol—continue to act as independent contributors to CVD in patients with diabetes. Clustering of metabolic risk factors, called the *metabolic syndrome*, occurs commonly in type 2 diabetes. The onset of hyperglycemia in patients with the metabolic syndrome appears to accelerate atherogenesis, possibly by enhanced formation of glycosylated proteins and advanced glycation products and/or by increasing endothelial dysfunction. These direct consequences of hyperglycemia probably contribute to the microvascular disease underlying nephropathy and retinopathy, and they may promote macrovascular disease as well.

Predisposing Risk Factors

Several predisposing factors simultaneously affect the development of CVD and diabetes mellitus. Among these concomitant factors are obesity, physical inactivity, heredity, sex, and advancing age. The mechanisms whereby they predispose to chronic diseases are complex and often overlapping. To some extent, these predisposing factors exacerbate the major risk factors: dyslipidemia, hypertension, and glucose tolerance; and they may cause CVD and diabetes mellitus through other pathways as well. To a large extent, both CVD and diabetes must be prevented through control of the predisposing risk factors. Modification of life habits is at the heart of the public health strategy for prevention of CVD and diabetes mellitus. High priorities are the prevention (or treatment) of obesity and promotion of physical activity. Drug therapy nonetheless may be required to control the metabolic risk factors, particularly when they arise from genetic aberration and aging. Effective drugs are currently available for treatment of hypertension and dyslipidemia. Hypoglycemic agents

also are available for treatment of type 2 diabetes, but new pharmacological strategies are under investigation for more effective treatment and prevention.

Insulin Resistance and the Metabolic Syndrome

Most patients with type 2 diabetes have insulin resistance. Indeed, insulin resistance seems to predispose to both CVD and diabetes. Research suggests that insulin resistance is a multisystem disorder that induces multiple metabolic alterations. Factors that contribute to insulin resistance are genetics, obesity, physical inactivity, and advancing age. Patients with insulin resistance often have abdominal obesity. Metabolic risk factors that occur commonly in patients with insulin resistance are atherogenic dyslipidemia, hypertension, glucose intolerance, and a prothrombotic state. Each of these risk factors are reviewed briefly below.

Atherogenic Dyslipidemia

Atherogenic dyslipidemia is characterized by 3 lipoprotein abnormalities: elevated very-low-density lipoproteins (VLDL), small LDL particles, and low high-density-lipoprotein (HDL) cholesterol (the lipid triad). The lipid triad occurs frequently in patients with premature CHD and appears to be an atherogenic lipoprotein phenotype independent of elevated LDL cholesterol. Most patients with atherogenic dyslipidemia are insulin resistant. Atherogenic dyslipidemia in diabetic patients often is called diabetic dyslipidemia. Many patients with atherogenic dyslipidemia also have an elevated serum total apolipoprotein B. Growing evidence suggests that all of the components of the lipid triad are independently atherogenic. Together they represent a set of lipoprotein abnormalities besides elevated LDL cholesterol that promote atherosclerosis.

Hypertension

Hypertension is a well-established major risk factor for CVD. It increases risk for both CHD and stroke and contributes to diabetic nephropathy. Several investigators report a positive association between insulin resistance and hypertension; this finding suggests that elevated blood pressure deserves to be listed among the components of the metabolic syndrome. Hypertension nonetheless is a multifactorial disorder (see text), and the mechanistic connections between insulin resistance and hypertension are largely conjectural; even so, evidence for a causal link is growing. When hypertension coexists with overt diabetes, which it commonly does, the risk for CVD, including nephropathy, is doubly increased.

Elevated Plasma Glucose

For several years after onset of insulin resistance, fasting and postprandial glucose levels typically are normal. During this period, pancreatic ß-cells are able to increase insulin secretion in response to insulin resistance and thereby maintain normal plasma glucose levels. In some people, however, insulin secretion declines with aging, and elevated glucose concentrations appear. The first abnormality in plasma glucose in patients with insulin resistance is IFG (or

impaired glucose tolerance). The presence of IFG usually accompanies long-standing insulin resistance. It is currently estimated that 13.4 million adults, 7.0% of the US population, have IFG. Many prospective studies show that IFG (or impaired glucose tolerance) is a risk factor for CVD; the degree of independence as a risk factor, however, is uncertain, because IGF commonly coexists with other components of the metabolic syndrome. A patient with IFG nonetheless must be considered at risk for both CVD and type 2 diabetes. As already indicated, once categorical hyperglycemia develops, it counts as an independent risk factor for CVD.

Prothrombotic State

A newly recognized component of the metabolic syndrome is a prothrombotic state. Patients with insulin resistance frequently manifest several alterations in coagulation mechanisms that predispose them to arterial thrombosis. These alterations include increased fibrinogen levels, increased plasminogen activator inhibitor-1, and various platelet abnormalities.

LDL Cholesterol and Atherogenesis in Diabetic Patients

An elevated concentration of serum LDL cholesterol is a major risk factor for CHD. In fact, some elevation of LDL cholesterol appears to be necessary for the initiation and progression of atherosclerosis. In populations having very low LDL cholesterol levels, clinical CHD is relatively rare, even when other risk factors—hypertension, cigarette smoking, and diabetes—are common. In contrast, severe elevations in LDL cholesterol can produce full-blown atherosclerosis and premature CHD in the complete absence of other risk factors.

The view has been expressed that most patients with diabetes do not have an elevated serum LDL cholesterol; if not, a high LDL serum cholesterol would not be a common risk factor in patients with diabetes. It is true that most patients who have diabetes do not have marked elevations of LDL cholesterol, but these patients nonetheless carry high enough levels to support the development of atherosclerosis. A role for LDL in hyperglycemic patients became apparent in recent clinical trials, e.g., the Scandinavian *Simvastatin* Survival Study (4S), the Cholesterol and Recurrent Events (CARE) trial, and the Long-Term Intervention with *Pravastatin* in Ischemic Disease (LIPID). In all of these trials, aggressive LDL-lowering therapy reduced recurrent CHD events in patients with diabetes.

Cigarette Smoking

Cigarette smoking is a leading risk factor for CVD. Patients with diabetes who are smokers are doubly at risk. Unfortunately, many patients continue to smoke despite having diabetes; for these patients, the benefits that can be derived from modifying other risk factors are mitigated.

Physical inactivity

An inactive lifestyle is a risk factor for coronary heart disease. Regular, moderate-

to-vigorous physical activity helps prevent heart and blood vessel disease. The more vigorous the activity, the greater your benefits. However, even moderate-intensity activities help if done regularly and long term. Exercise can help control blood cholesterol, diabetes and obesity, as well as help lower blood pressure in some people.

Cardiovascular Diseases Combined

Most of the reported studies relating physical activity to CVD have reported CVD mortality as an endpoint; two also reported on nonfatal disease, and one reported on CVD hospitalization. Seven cohort studies evaluated the association between level of physical activity and the risk of total CVD. All relied on a single point-in-time estimate of physical activity, in some cases assessed as long as 26 years before the end of the observational period, and four had follow-up periods of > 14 years. Four of the seven studies found both an inverse association and a dose-response gradient between level of physical activity and risk of CVD outcome.

One study among men found an inverse association among the moderately active group but less of an effect in the vigorously active group. One study of women 50–74 years of age found no relationship of physical activity with CVD mortality. Five large cohort studies have related cardiorespiratory fitness to the risk of CVD mortality, but only one provided a separate analysis for women. Each of these studies demonstrated an inverse dose-response relationship between level of cardiorespiratory fitness and CVD mortality. Three of the five studies relied on a maximal or near-maximal exercise test to estimate cardiorespiratory fitness. One study (Blair et al. 1995) demonstrated that men with low cardiorespiratory fitness who became fit had a lower risk of CVD mortality than men who remained unfit. Taken together, the major cohort studies indicate that low levels of physical activity or cardiorespiratory fitness increase risk of CVD mortality. Findings seem to be more consistent for studies of cardiorespiratory fitness, perhaps because of its greater precision of measurement, than for those of reported physical activity. The demonstrated dose-response relationship indicates that the benefit derived from physical activity occurs at moderate levels of physical activity or cardiorespiratory fitness and increases with increasing levels of physical activity or higher levels of fitness.

Coronary Heart Disease

Numerous studies have examined the relationship between physical activity and CHD as a specific CVD outcome. Reviews of the epidemiologic literature (Powell et al. 1987; Berlin and Colditz 1990; Blair 1994) have concluded that physical activity is strongly and inversely related to CHD risk. Although physical Exertion may transiently increase the risk of an acute coronary event among persons with advanced coronary atherosclerosis, particularly among those who Do not exercise regularly. Physically active people have a substantially lower overall risk for major coronary events.

Other factors contribute to heart disease risk

Socioeconomic factors and cardiovascular disease

Many of the major risk factors for coronary disease have been identified. Researchers are still learning about different modifiable factors that may influence cardiovascular diseases. Socioeconomic (SES) status may provide a new focus. The principal measures of SES have been *education, occupation, and income or combinations of these. Education* has been the most frequent measure because it does not usually change (as occupation or income might) after young adulthood, information about education can be obtained easily, and it is unlikely that poor health in adulthood influences level of education. However, other measures of SES have merit, and the most informative strategy would incorporate multiple indicators of SES. A variety of psychosocial measures--for example, certain aspects of *occupational status*--may be important mediators of SES and disease. The hypothesis that high job strain may adversely affect health status has a rational basis and is supported by evidence from a limited number of studies. There is a considerable body of evidence for a relation between socioeconomic factors and all-cause mortality. These findings have been replicated repeatedly for 80 years across measures of socioeconomic level and in geographically diverse populations. During 40 years of study there has been a consistent inverse relation between cardiovascular disease, primarily coronary heart disease, and many of the indicators of SES. Evidence for this relation has been derived from prevalence, prospective and retrospective cohort studies. Of particular importance to the hypothesis that SES is a risk factor for cardiovascular disease was the finding by several investigators that the patterns of association of SES with coronary disease had changed in men during the past 30 to 40 years and that SES has been associated with the decline of coronary mortality since the mid-1960s. However, the declines in coronary mortality of the last few decades have not affected all segments of society equally. There is some evidence that areas with the poorest *socio-environmental* conditions experience later onset in the decline in cardiovascular mortality. A number of studies suggest that poor living conditions in childhood and adolescence contribute to increased risk of arteriosclerosis.

Psychosocial factors and heart disease

There is clear and convincing evidence that psychosocial factors contribute significantly to coronary disease as evidenced by data relating risk to (1) depression, (2) anxiety, (3) personality factors and character traits, (4) social isolation, and (5) chronic life stress. Mechanisms underlying these relationships manifest either through behavioral choices of factors which contribute to adverse health effects (e.g. poor diet, smoking); or through direct pathophysiological mechanisms (e.g. neuroendocrine surges and platelet activation). Extensive primate research shows that chronic psychosocial stress leads to exacerbation of

coronary atherosclerosis, transient endothelial dysfunction and even necrosis, probably from excessive sympathetic nervous system activation. Primate evidence also shows that psychosocial stress induces ovarian dysfunction, hypercortisolemia and excessive sympathetic adrenergic activation in premenopausal women, leading to accelerated atherosclerosis. In animals, acute stress triggers myocardial ischemia, promotes arrhythmogenesis, stimulates platelet overactivity and increases blood viscosity through hemoconcentration, leading to coronary vasoconstriction.. Hyperresponsiveness of the sympathetic nervous system, manifested by elevated heart rate and blood pressure surges in response to psychological stimuli, is intrinsic in some individuals, contributing to accelerated carotid atherosclerosis in humans and exacerbated coronary and carotid atherosclerosis in primates. When psychosocial stresses tend to cluster together, risk for cardiac events is often substantially elevated, equaling or exceeding that associated with standard biomedical risk factors for coronary disease such as hypertension and hypercholesterolemia.

Individual response to stress is widely different between people to. Scientists have noted a relationship between coronary heart disease risk and stress in a person's life, their health behaviors and socioeconomic status. These factors may affect established risk factors. *For example*, people under stress may overeat, start smoking or smoke more than they otherwise would.
Stress over the long term has been shown in several studies to raise blood cholesterol levels. One way that stress may do this is by affecting your habits.

Alcohol — Drinking too much alcohol can raise blood pressure, cause heart failure and lead to stroke. It can contribute to high triglycerides, cancer and other diseases, and produce irregular heartbeats. It contributes to obesity, alcoholism, suicide and accidents. The risk of heart disease in people who drink moderate amounts of alcohol (an average of one drink for women or two drinks for men per day) is lower than in nondrinkers. One drink is defined as 1-1/2 fluid ounces (fl oz) of 80-proof spirits (such as bourbon, Scotch, vodka, gin, etc.), 1 fl oz of 100-proof spirits, 4 fl oz of wine or 12 fl oz of beer. It's not recommended that nondrinkers start using alcohol or that drinkers increase the amount they drink. Alcohol intake increases HDL ("good") cholesterol but does not lower low-density lipoprotein ("bad") cholesterol. We don't know for certain whether alcohol also reduces the risk of heart disease.

Controversial attributing factors The role of estrogens, homocysteine, thrombotic and inflammatory factors is currently the subject of considerable research. It seems likely that a certain genetic constitution enhances the susceptibility to the effects of other risk factors. New candidate genes are being suggested daily. Until now, no clearly decisive results have been achieved in determining the relations between the investigated genetic polymorphisms and the occurrence of cardiovascular disease. The consumption of foodstuffs that are rich in anti-oxidants seems to reduce the risk of cardiovascular disease, but

randomized research into the effects of anti-oxidants as food supplements suggests that this does not affect the development of cardiovascular disease. Homocysteine levels are strongly influenced by dietary intake of folic acid and B vitamins. Insuring adequate intake of these vitamins may help lower homocysteine levels

Prevention of cardiovascular diseases

Thanks to the ever increasing trends in the modern public health to study and research the complex various factors contributing to cardiovascular diseases, and identifying more and more contributing factors for the *number one killer* disease in developed world there is an ever increase in the intervention measures that health care systems have to deal with the disease.

The following is a summery of the recent recommendation for different subgroups of patients with increased risk of developing cardiovascular disease and for those who are already diagnosed.(medical and surgical interventions of acute MI and heart failure are beyond the scope of this reveiw).

Recommendations for all patients

Healthy lifestyle

Advice concerning the benefits of smoking cessation, physical activity and healthy dietary choices should be given at a population and individual level. These measures are considered as *first-line* in any management decisions.

A.Cessation of smoking

The corner stone in primary prevention There is extensive evidence that smoking is strongly related to mortality, largely because of an increased risk of CHD and stroke. Furthermore, smoking cessation has been shown to decrease this risk in patients with and without established CHD. In patients with peripheral vascular disease or stroke, smoking cessation is associated with improved exercise tolerance and survival, and decreased rates of limb amputation and recurrent stroke.

wider dissemination of self-help materials, such as smoking-cessation booklets, hold the potential for assisting a substantial number of smokers who might not seek help in quitting smoking through more formal methods. In addition, the cost-effectiveness of smoking-cessation programs may be enhanced by targeting specific populations (e.g., smoking-cessation manuals tailored to pregnant women) and developing programs with a follow-up or maintenance component that use a combination of multiple interventions..

Physician intervention can be an effective strategy for smoking prevention and cessation. Physicians can counsel persons in high-risk groups, including

pregnant women and adolescents whose other behaviors (e.g., alcohol use and poor school performance) indicate they are more likely to use tobacco. Counseling effectiveness can be increased by direct face-to-face advice and suggestions, setting of a target date for quitting, scheduled reinforcement, provision of self-help materials, referral to community programs, and drug therapy when used as an adjunct to other behavioral interventions. Smoking-cessation counseling should receive the highest priority as a preventive intervention and recommended that physicians 1) obtain a complete history of tobacco use for all adolescent and adult patients and offer counseling on a regular basis to all tobacco users.

Effective community-based tobacco-control programs, stimulate community involvement by identifying major community groups and organizations that can support interventions. Smoking-control activities in communities should encompass health-care providers, worksites, cessation resources and services, and public education.

The proportion of smokers who have quit is been consistently higher for males than for females, for whites than for blacks, for older smokers than for younger smokers, and for college graduates than for persons with less than a high school education.

The achievement of long-term health and economic benefits of reducing the nation's overall smoking rate also requires intensive smoking-prevention efforts. In particular, each year, more than 1 million young persons start to smoke, adding an estimated $10 billion during their lifetimes to the cost of health care in the United States. A multicomponent approach to prevent initiation among youths should be coupled with school-based tobacco-use prevention programs and include 1) mass media campaigns to target high-risk groups, 2) increased excise taxes on tobacco products, 3) increasing the minimum age for sale of tobacco products, 4) prohibiting the distribution of tobacco product samples to minors, 5) elimination or severe restriction of tobacco product advertising and promotion to which youth are likely to be exposed, 6) restricting the sale of tobacco products through vending machines, and 7) enforcing tobacco access laws for minors.

b. Exercise

While there is limited evidence of the value of exercise in ***primary prevention*** of cardiovascular disease, there is strong observational evidence that moderate, regular physical activity reduces the risk of both CHD and stroke, and that the risk is increased in people with a sedentary lifestyle. For ***secondary prevention*** after AMI, two meta-analyses of exercise-based rehabilitation have shown reductions in mortality of between 20% and 25% (absolute risk reduction [ARR], 3.1%) at 3-year follow-up, although many of the trials allowed other risk-factor intervention as well., While these data must be interpreted with caution, prescribing a moderate degree of regular physical exercise is consistent with

published evidence.

c. Diet

Cohort studies have shown that eating fruit and vegetables reduces the risk of heart attack and stroke. Eating fish or taking fish oil capsules has been shown to reduce IHD mortality, though the dose of omega-3 oil required is 10 times more than that consumed by fish-eaters.

Mediterranean diet decreased mortality by 30% at after AMI (ARR, 4.0%).In addition, a modest intake of fish (as little as 35 g daily) appears to decrease the relative risk of AMI. Following general advice to decrease the intake of saturated fats and cholesterol and increase the intake of polyunsaturated fats favorably affects serum lipid levels and decreases the likelihood of CHD.
Finally, weight maintenance education should be part of routine advice for the general population, but is particularly important in patients at increased risk of cardiovascular events.

Regular fresh fruit and vegetables are believed to be protective but not clear to what extent, and may be part of an overall lifestyle pattern. The antioxidant phytochemicals, particularly flavonoids (found in red wine, black tea, beer), appear to be protective, as are the vegetable proteins soy, and seitan. Increased intake in dietary fibre from cereals reduces risk, but can interfere with the absorption of certain vitamins and minerals. Foods rich in phytochemicals and vitamins, are also rich in fibre.

d. Stress

There is "no strong or consistent evidence for a causal association between chronic life events, work-related stressors (job control, demands and strain), type A behaviour patterns, hostility, anxiety disorders or panic attacks and CHD". However, there was strong and consistent evidence of an independent and causal association between depression, social isolation and the prognosis of CHD and, importantly, the impact of these was of a similar order to conventional risk factors such as smoking. It is therefore crucial that these psychosocial factors are considered during *individual* CHD risk assessments.

Recommendations for patients with established vascular disease

1. Normotensive patients with a history of cardiovascular disease

The HOPE, PROGRESs_and, more recently, EUROPA studies have examined the effects of *preventive treatment* with ACE inhibitors in normotensive high-risk patients. In the HOPE study, patients with CHD, peripheral vascular disease, stroke, or diabetes (types 1 or 2) and an additional risk factor were randomly allocated to receive *ramipril* 10 mg daily or placebo. Patients were included

irrespective of a history of hypertension, but those with blood pressure greater than 140/90 mmHg or with a specific indication for treatment with an ACE inhibitor (e.g., CCF) were excluded. The 3/1 mmHg lower blood pressure in the *ramipril* group at the end of the study was unlikely to explain the highly significant 22% reduction in the combined endpoint of cardiovascular death, stroke or heart attack.

In the PROGRESS study, patients with a previous history of stroke or TIA were randomly allocated to *perindopril* 4 mg ± *indapamide* 2.5 mg versus placebo, whether there was a history of hypertension or not. When given together this combination *reduced the risk* of recurrent stroke (fatal or non-fatal) and major vascular events in both normotensive and hypertensive patients with this background. There was also a significant reduction in major coronary events (26%) and the development of heart failure (26%) in these patients with underlying cerebrovascular disease. The magnitude of blood pressure reduction in the active treatment group was greater in the PROGRESS study (9/4 mmHg) than in the HOPE study (3/1 mmHg), making it less clear as to how much of the benefit seen in the PROGRESS study was independent of blood pressure reduction alone.

The recently published EUROPA study looked at patients with known ischaemic heart disease, and participants were randomly allocated to receive *perindopril* 8 mg or placebo, independent of whether or not they had a history of hypertension. At 5 years, there was a significant 20% reduction in cardiovascular mortality, infarction and cardiac arrest in patients who received *perindopril*, with a blood pressure difference of 5/2 mmHg between the groups.

It appears that, in patients with a history of CHD or cerebrovascular disease, treatment with a high dose *ramipril- or perindopril-based regimen* will improve outcomes whether or not there is a history of hypertension, and that at least some of these benefits are independent of blood pressure reduction alone.

In the immediate post-infarct management of normotensive patients, a mortality benefit in the short term has also been demonstrated with *β-blockers and ACE inhibitors* (particularly in patients with associated heart failure), with less robust evidence for calcium channel blockers, *verapamil and diltiazem.*

2. Patients with elevated blood pressure and a history of cardiovascular disease

While epidemiological studies have established that raised blood pressure is a major risk factor for cardiovascular events in patients with a history of AMI, until recently there has been no systematic review that specifically examines blood pressure reduction in patients with established CHD, nor in those with peripheral vascular disease; however, the results of the HOPE, PROGRESS and EUROPA studies are applicable to patients with hypertension. In the recommendations of the National Heart Foundation, the benefits of blood pressure lowering in patients

with CHD have been extrapolated mostly from *primary prevention* trials and from studies of patients after AMI. Evidence of event reduction exists for patients taking *calcium channel blockers, diuretics and β-blockers, and ACE inhibitors*. In patients with elevated blood pressure and a history of stroke or TIA, the evidence is strongest for the use of ACE inhibitors (*ramipril* 10 mg; and *perindopril* 4 mg when given with *indapamide* 2.5 mg), diuretics and β-blockers. .

The results of treatment with ACE inhibitors, diuretics or calcium channel blockers were comparable. It should be noted, however, that there was an increased rate of development of diabetes mellitus in the thiazide diuretic treatment arm. In view of the impact of diabetes on cardiovascular event rates, this finding may have implications for cardiovascular disease beyond the 5-year treatment period covered by the trial.

3. Patients with dyslipidaemia and a history of cardiovascular disease

There is strong RCT evidence that lowering cholesterol levels decreases cardiovascular mortality and morbidity in patients who have been diagnosed with an acute coronary syndrome or myocardial infarction, even if cholesterol levels are normal. The most substantial data are from studies of *simvastatin* and *pravastatin*, intensive lipid lowering with *atorvastatin* 80 mg improves outcomes more than moderate lipid lowering in patients with acute coronary syndromes and cholesterol levels less than 6.2 mmol/L. The Heart Protection Study provides the most complete information of the benefits of lowering cholesterol level in a wide range of circumstances. Both men and women with total cholesterol levels greater than 3.5 mmol/L and with a history of cardiovascular disease (including those with a history of coronary disease, cerebrovascular disease, or peripheral vascular disease) achieved a significant reduction in major vascular events ($P < 0.001$) irrespective of the starting cholesterol level.

In men with low levels of HDL cholesterol and a history of CHD, *gemfibrozil* significantly reduced the risk of major cardiovascular events, in the absence of an effect on LDL cholesterol level.

In patients with diabetes and CHD, the data are strongest for the use of *statins*, but, again, in patients with low levels of HDL cholesterol *gemfibrozil* is efficacious. To date, this evidence has been derived from subgroup analyses. In RCTs, it has been shown that both *pravastatin* and *simvastatin* reduce the incidence of stroke in patients with CHD, but in those without CHD the evidence is strongest for *simvastatin*. There are no "head-to-head" outcome studies of *statins* versus *fibrates*.

Recommendations for patients with diabetes without known cardiovascular disease

1. Patients with diabetes and "normal" blood pressure

In patients with diabetes, "normal" blood pressure is arbitrarily defined as being less than 130/85 mmHg and "ideal" blood pressure as less than 120/80 mmHg. Treatment of low-risk patients with diabetes (i.e. those who have no additional cardiovascular risk factors) with an ACE inhibitor to prevent future CHD events is not supported by current data. *Observation with repeated measurement of blood pressure at least annually is recommended.*

2. Patients with diabetes and elevated blood pressure

A systematic review of RCTs has shown that ACE inhibitors, diuretics, calcium channel blockers and β-blockers are all *effective in primary prevention* of cardiovascular events in patients with diabetes and hypertension. There is no clear evidence that any of these classes is more effective than another in event reduction, and currently drugs of all of these classes are recommended to treat blood pressure in patients with diabetes. Despite this, an apparent greater reduction in major cardiovascular events (including heart failure) occurring with ACE inhibitors, compared with some calcium channel blockers, has led us to list calcium channel blockers as second-line therapy. In addition to reducing cardiovascular events, ACE inhibitors have a major role in renal protection in patients with type 1 diabetes and hypertension. Similar protection has recently been shown with the AIIRAs *irbesartanand losartan*, including patients with type 2 diabetes and left ventricular hypertrophy.

3. Lowering cholesterol level in patients with diabetes

Patients with diabetes with a total cholesterol level greater than 3.5 mmol/L had significantly fewer major vascular events ($P < 0.0001$) when taking *simvastatin* 40 mg, whether or not they had a prior history of CHD. To date, this is the largest intervention trial of *statin* therapy in patients with diabetes and thus should be considered the definitive trial. These data support the use of a *statin* for both *primary and secondary prevention* of major vascular events in patients with diabetes. Furthermore, three large primary prevention RCTs using *lovastatin, gemfibrozil and bezafibrate* have each shown a benefit in preventing cardiovascular events. Thus, a predominant elevation of total or LDL cholesterol levels indicates a *statin* is appropriate initial therapy, whereas a *fibrate* could be an appropriate choice in patients with low levels of HDL cholesterol and raised triglyceride levels. When treating combined hyperlipidaemia, both classes of drug may be required, but there are no outcome data from using this approach and practitioners should exercise caution in prescribing this combination.

4. Cardiovascular prevention with other therapies

In patients with diabetes and dyslipidaemia (total cholesterol level > 5.2 mmol/L and HDL cholesterol level 0.9 mmol/L), the use of *ramipril* in addition to other therapies should be advocated in diabetic patients with dyslipidaemia or other cardiovascular risk factors.

Recommendations for patients with non-diabetic renal disease

1. Patients with non-diabetic renal disease and "normal" blood pressure

Renal insufficiency is a well described predictor of cardiovascular outcomes. Hypertension in patients with renal disease is defined as blood pressure greater than 130/85 mmHg, although observational studies suggest that even a lower blood pressure confers an increased risk. Despite this, there is no RCT of antihypertensive therapy showing treatment benefit if blood pressure is below this threshold. Ongoing observation with repeated measurement of blood pressure every 6 months is currently recommended for normotensive patients with non-diabetic renal disease.

2. Patients with non-diabetic renal disease and hypertension

The benefits of treating hypertension in patients with established renal disease have largely been studied with surrogate endpoints, and the effects of lowering blood pressure on cardiovascular outcomes have not been specifically assessed. Nevertheless, patients with renal dysfunction are at high risk of CHD and it is reasonable to extrapolate from this that aggressive blood pressure lowering will confer a substantial benefit.

Published data support the use of *ACE inhibitors* as first-line treatment for hypertension, with greater demonstrated efficacy in reducing proteinuria than calcium channel blockers. Further, in a meta-analysis of a number of clinical trials, *ACE inhibitors* were more effective than other agents in delaying the development of end-stage renal disease; however, it could not be determined whether this was due to the lower blood pressure achieved with *ACE inhibitors* or to effects independent of blood pressure. *β-Blockers* and diuretics are also recommended. If calcium channel blockers are used they should be considered as second-line therapy after *ACE inhibitors.*

Although renal function deteriorated markedly after a first AMI, it was significantly preserved by taking the ACE inhibitor *captopril.* Patients after a first anterior-wall AMI were allocated at random to receive *captopril* (up to 75 mg daily) or placebo, after completion of a streptokinase infusion. Renal function determined by calculating glomerular filtration rate was found to decline by 5.5 mL/min within 1 year versus only 0.5 mL/min in the *captopril* group ($P < 0.05$). The beneficial effects of *captopril* were most pronounced in patients with the most compromised renal function at baseline.

Combination treatment was found to safely retard the progression of non-diabetic renal disease compared with monotherapy; however, as some patients taking combined therapy reached the combined endpoint, further research on strategies for complete management of progressive non-diabetic renal disease is needed.

3. Lowering cholesterol level in patients with non-diabetic renal disease

Specific trials of lipid-lowering therapy have not been conducted in patients with non-diabetic renal disease. Thresholds for intervention have been derived by consensus and recommendations for the choice of agents have been based on the lipid-lowering characteristics of specific therapies.

The approach for other high-risk patients

Over the past decade, it has been recommended that the intensity of risk-factor management be governed by a patient's absolute risk of a CHD event. However, patients with mild levels of multiple risk factors may be at high risk because of the exponential additive contribution of each risk factor, whereas other patients may have an overall low risk even if they have one markedly abnormal risk factor.

1. High-risk patients with raised blood pressure

A number of systematic reviews have shown a reduction in total mortality, cardiovascular death, stroke, major coronary events and CCF in patients taking β-blockers, diuretics, ACE inhibitors or calcium channel blockers. One unblinded RCT in 6600 people aged 70–84 years, comparing diuretics and/or β-blockers versus calcium channel blockers versus ACE inhibitors, showed no significant difference in blood pressure control or cardiovascular morbidity and mortality. The ALLHAT study, involving hypertensive patients with at least one other CHD risk factor, supports these findings. When the primary outcome was considered (fatal CHD or non-fatal AMI), diuretic-based therapy (*chlorthalidone*) was of similar efficacy to either therapy with a calcium channel blocker (*amlodipine*) or an ACE inhibitor (*lisinopril*). In fact, patients taking *amlodipine* had an increased risk of CCF (relative risk, 1.38; 95% CI, 1.25–1.52) and patients taking *lisinopril* had a higher risk of combined cardiovascular disease, stroke and CCF. As *amlodipine* is a *dihydropyridine* calcium channel blocker, it may not be possible to extrapolate these results to the *non-dihydropyridine* calcium channel blockers.

2. Lowering cholesterol level in patients at high risk of a cardiovascular event

Until recently, there was no evidence that lowering cholesterol level reduces total mortality in non-diabetic patients without cardiovascular disease, although systematic reviews and RCTs had shown that cholesterol reduction improves cardiovascular outcomes in high-risk populations. The benefit is related to baseline risk and extent of cholesterol reduction rather than initial cholesterol level.

The benefits of lipid reduction for hypertensive patients with multiple cardiovascular risk factors. Treatment with *atorvastatin* 10 mg conferred a 36% reduction in fatal CHD and non-fatal AMI compared with placeb. The benefits of lipid reduction were also evident among non-diabetic patients.

A total cholesterol level greater than 5 mmol/L is the current recommended

threshold for treatment in patients with associated risk factors or vascular disease.

The approach for patients at low risk of a cardiovascular event

Patients who are not in any of the above categories are at low risk of a cardiovascular event. There is a more liberal threshold for intervention in this group in the knowledge that the treatment benefits will be smaller, but the recommendations for choice of therapy to lower blood pressure and lipid levels are identical to those in higher-risk patients.

1. Blood pressure management

We routinely adopt a more proactive approach for monitoring blood pressure than the current guidelines, which advocate that low-risk patients whose blood pressure is considered normal by current criteria should have blood pressure measurements either every 5 years (age < 60 years) or every 1–2 years (age > 60 years). Current clinical practice would also be at variance with the guideline recommendations that *drug therapy and lifestyle modification for hypertension* should only be introduced in patients under 60 years if their systolic blood pressure is greater than 180 mmHg or diastolic blood pressure greater than 100 mmHg, or in those over 60 years whose systolic blood pressure is greater than 160 mmHg.

2. Lipid management

Patients with normal lipid levels should be assessed every 5 years until middle age and then every 1–2 years. In the absence of other risk factors triggering a lower threshold for treatment, lipid-lowering therapy with a *statin* should be commenced for patients with predominant hypercholesterolaemia (total cholesterol > 8.0 mmol/L or total cholesterol : HDL cholesterol ratio > 8.0), or with a *fibrate* for patients with low HDL cholesterol and high triglyceride levels. (At present, the reimbursement criteria of the Pharmaceutical Benefits Schedule are at variance with National Heart Foundation guidelines).

The approach for patients with macro- or microalbuminuria associated with diabetes or hypertension

The finding of microalbuminuria (urinary albumin excretion 20–200 µg/min) or macroalbuminuria (urinary albumin excretion > 200 µg/min) should prompt a search for the presence of diabetes, hypertension or renal disease. If diabetes is present, the use of ramipril is appropriate for cardiovascular risk reduction. Furthermore, there is good evidence to support the use of ACE inhibitors for renal risk reduction in normotensive patients with diabetes (type 1 or type 2) and microalbuminuriaand hypertensive patients with type 2 diabetes, and the use of AIIRAs (*irbesartan* and *losartan*) in patients with type 2 diabetes.

Other interventions

1. Antiplatelet therapies (aspirin, dipyridamole or clopidogrel)

Aspirin (75–150 mg/day) has been shown to have significant benefit for patients at high risk of cardiovascular disease, particularly in secondary prevention, although blood pressure should be tightly controlled to minimize the risk of hemorrhagic stroke. It must be recognized, however, that the benefits of *aspirin* are not clear in older patients (> 70 years) with no previous cardiovascular events who, primarily due to age, remain at high risk of cardiovascular disease. This is highlighted by the recent *FDA* decision not to list primary prevention of cerebrovascular disease as an indication for aspirin in the elderly and to strongly support proposals for the conduct of such trials. *The risks associated with gastrointestinal and cerebral bleeding* in older patients may offset any cardiovascular protection benefits. The American Diabetes Association recommends the use of *aspirin* for patients with diabetes over the age of 30 years, but there is no evidence of benefit in primary prevention in low-risk subjects.

Alternative or additional *antithrombotic* therapies such as *clopidogrel* or *dipyridamole* (stroke or TIA only) may be required if aspirin is not tolerated or the patient experiences recurrent cardiovascular events while taking aspirin.

It is beyond the scope of this review of cardiovascular prevention measures to focus on the management of acute coronary syndromes. However, it is important to highlight the results of a recent trial using combination *antiplatelet therapy* in patients with acute coronary syndromes: initiating therapy during the acute management phase in hospital was shown to have benefits up to 1 year after the initial presentation. Patients with acute coronary syndromes who were given a loading dose of 300 mg of *clopidogrel* followed by ongoing treatment with 75 mg daily for 9 months, in addition to their usual therapy (including *aspirin*), had a 20% reduction in the combined endpoint of cardiovascular death, AMI, and stroke (ARR, 2.1%). Thus, many patients who leave hospital after an admission with unstable angina or non-ST elevation myocardial infarction will be receiving *clopidogrel* in addition to aspirin as combined *antiplatelet therapy* for *atherothrombosis*, which should be continued as long-term therapy.

A 27% relative risk reduction (ARR, 3.0%) in the combined endpoint of death, AMI and stroke at 1 year with the use of *clopidogrel* added to conventional therapy (including aspirin) after placement of a coronary *stent*. Once again, early treatment translates into long-term preventive therapy, and thus a case can be made for the use of combination *antiplatelet therapy* (*aspirin* and *clopidogrel*) for preventing ischaemic events in appropriate patients. Definitive long-term trials of this combination to prevent events in patients with cardiovascular disease (but who have not presented with an acute coronary syndrome), or to avoid the need for coronary artery *stenting*, are currently under way.

2. Anticoagulation

Long-term anticoagulation to reduce thromboembolism may be required for patients with paroxysmal or chronic atrial fibrillation, proteinuria greater than 3 g/day, and those with a history of extensive anterior infarction or severe CCF.

Summery and the future

Cardiovascular diseases are the increasingly listed as the number one disease that kills human being's despite the great and ever growing arrays of intervention measures in health care system. And continue to be a major burden on health care system and in the national concerns of the developed world.

The major risk factors that contribute to the disease: hypertension, obesity and increased cholesterol, smoking, diabetes, psychosocial and socioeconomic factors are being increasingly subjects for modifications and new strategies of intervention thanks to ever-growing interest of new research to identify more attributing risk factors and to evaluate more the well-known and established ones.

It's a great field for health care services in general and for public health specially in the future to conduct more studies and researches to lead other studies and effort of other fields to let us better deal with cardiovascular diseases. Without the knowledge of the disease and its associations its not reliable to test new drugs or to recommend other medical therapies .

The worldwide tendency for CHD mortality to decline might suggest that "tomorrow is already here." While this trend is encouraging and, in countries where it could be analyzed, seems to be the result of favorable changes in lifestyles, it is less certain whether there has been a concomitant decline in CHD incidence. In any case, there are no grounds for complacency because even in countries such as the United States, prevention has a long way to go. Intervention studies and collateral evidence have left no reasonable doubt that CHD is preventable. The problem lies in translating this knowledge into action. On the whole, the forces supporting action have been gaining over those slowing or obstructing it, but there still exists strong resistance, ranging from frank opposition to disinterest, especially regarding cholesterol. The most serious among an array of claims is that low or lowering serum cholesterol leads to an increase in noncardiovascular disease, in particular cancer risk. According to the best evidence currently available, the excess cancer risk, if it exists, is small and confined to persons with very low cholesterol levels that are rare or will rarely be reached with preventive treatment; the excessive risk said to be related to noncancer and noncardiovascular diseases, including traumatic deaths, is probably entirely due to confounding by preexisting disease, detrimental habits such as smoking, or excessive drinking and influences related to social class.

The chances are that the future will bring advances in scientific knowledge of

disease mechanisms, putting preventive measures on even stronger foundations. It is also likely that there will be a deepened understanding of the forces that determine individual and group attitudes and behaviors relating to the preservation of health. On the other hand, it is uncertain whether or to what extent future socioeconomic and political developments, in different parts of the world and cultures, will favor a climate in which healthy lifestyles can establish themselves. Competing demands coming from priority needs to control infectious diseases in some countries also must be taken into account. At this time, at the crossroads of change, it is hazardous to predict the direction in which the world is moving. However, as far as preventive medicine is concerned, there is no alternative to holding a steady course in the hope that the gains already made can be consolidated and extended into the future.

Murray CJL, Lopez A. Alternative Projections of Mortality and Disability by Causes 1990–2020: Global Burden of Disease Study. *Lancet* 1997;349:1498–1504.

Foot DK, Lewis RP, Pearson TA, Beller GA. Demographics and Cardiology, 1950–2050. J*ournal of the American College of Cardiology* 2000;35(No. 5, Suppl B):66B–80B.

Howard G, Howard VJ. Stroke Incidence, Mortality, and Prevalence.In:Gorelick PB, Alter M, editors. *The Prevention of Stroke.* New York, NY: The Parthenon Publishing Group; 2002:1–10.

Cooper R, Cutler J, Desvigne-Nickens P, et al. Trends and Disparities in Coronary Heart Disease, Stroke, and Other Cardiovascular Diseases in the United States. Findings of the National Conference on Cardiovascular Disease Prevention. *Circulation* 2000;102:3137–47.

Cooper R, Cutler J, Desvigne-Nickens P, et al. Trends and Disparities in Coronary Heart Disease, Stroke, and Other Cardiovascular Diseases in the United States. Findings of the National Conference on Cardiovascular Disease Prevention. *Circulation* 2000;102:3137–47.

Howard G, Howard VJ. Stroke Incidence, Mortality, and Prevalence. In:Gorelick PB, Alter M, editors. *The Prevention of Stroke.* New York, NY: The Parthenon Publishing Group; 2002:1–10.

Pathobiological Determinants of Atherosclerosis in Youth (PDAY)Research Group. Relationship of Atherosclerosis in Young Men to Serum Lipoprotein Cholesterol Concentrations and Smoking. *JAMA*1990;264:3018–24.

Kottke TE, Puska P, Salonen JT, Tuomilehto J, Nissinen A. Projected Effects of High-Risk Versus Population-Based Prevention Strategies in Coronary Heart Disease. *American Journal of Epidemiology* 1984;121:697–704.

Magnus P, Beaglehole R. The Real Contribution of the Major Risk Factors to the Coronary Epidemics: Time to End the "Only 50%" Myth. *Archives of Internal Medicine* 2001;161:2657–60.

Strasser T. Reflections on Cardiovascular Diseases. *Interdisciplinary Science Reviews* 1978;3:225–30.

Knowler WC, Barrett-Connor E, Fowler SE, et al and the Diabetes Prevention Program Research Group. Reduction in the Incidence of Type 2 Diabetes with Lifestyle Intervention or Metformin. *New England Journal of Medicine* 2002;346:393–403.

Goff DC Jr, Howard G, Russell GB, Labarthe DR. Birth Cohort Evidence of Primary Prevention of High Blood Pressure in the United States, 1887–1994. *Annals of Epidemiology* 2000;11:271–9. Institute of Medicine. *America's Vital Interest in Global Health.* Washington, DC: National Academy Press; 1997:44, 46.

PROGRESS Collaborative Group. Randomised trial of a perindopril-based blood-pressure-lowering regimen among 6105 individuals with previous stroke or transient ischaemic attack. *Lancet* 2001; 358: 1033-1041.

Heart Protection Study Collaborative Group. MRC/BHF heart protection study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomised placebo-controlled trial. *Lancet* 2002; 360: 7-22.

Halkjaer, J., Holst, C., Sorensen, T. I.A. (2003). Intelligence Test Score and Educational Level in Relation to BMI Changes and Obesity. *Obesity* 11: 1238-

Tang, M., Chen, Y., Krewski, D. (2003). Gender-related differences in the association between socioeconomic status and self-reported diabetes. *Int. J. Epidemiol.* 32: 381-385

Wooley, C S, Garner, D M (1994). Controversies in Management: Dietary treatments for obesity are ineffective. *BMJ* 309: 655-656

Martikainen, P. T, Marmot, M. G (1999). Socioeconomic differences in weight gain and determinants and consequences of coronary risk factors. *Am. J. Clin. Nutr.* 69: 719-726

Bild DE, Bluemke DA, Burke GL, et al: Multi-ethnic study of atherosclerosis: objectives and design. Am J Epidemiol 2002 Nov 1; 156(9): 871-81

Centers for Disease Control and Prevention: Surgeon General's report on physical activity and health CAPPP Group: The Captopril Prevention Project: a prospective intervention trial of angiotensin converting enzyme inhibition in the treatment of hypertension. J Hypertens 1990 Nov; 8(11): 985-90

CAPRIE Group: [New analysis of CAPRIE (Clopidogrel vs Aspirin in Patients at Risk of Ischemic Events) shows: myocardial infarct most effectively

Gurfinkel E, Bozovich G, Daroca A, et al: Randomised trial of roxithromycin in non-Q-wave coronary syndromes: ROXIS Pilot Study. ROXIS Study Group. Lancet 1997 Aug 9; 350(9075): 404-7.

Haffner SM, Lehto S, Ronnemaa T, et al: Mortality from coronary heart disease in subjects with type 2 diabetes and in nondiabetic subjects with and without prior myocardial infarction. N Engl J Med 1998 Jul 23; 339(4): 229-34.

Hegele RA: Angiotensin-converting enzyme (ACE) inhibition in the secondary prevention of vascular disease: the Heart Outcomes Prevention Evaluation (HOPE) Trial and its substudies. Curr Atheroscler Rep 2000 Sep; 2(5): 361-2.

Keil JE, Sutherland SE, Knapp RG, et al: Mortality rates and risk factors for coronary disease in black as compared with white men and women. N Engl J Med 1993 Jul 8; 329(2): 73-8.

Libby P: Changing concepts of atherogenesis. J Intern Med 2000; 247(3): 349-58.

National Institutes of Health: Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults--The Evidence Report. Obes Res 1998 Sep; 6 Suppl 2: 51S-209S.

Perry HM Jr, McDonald RH, Hulley SB, et al: Systolic Hypertension in the Elderly Program, Pilot Study (SHEP-PS): morbidity and mortality experience. J Hypertens Suppl 1986 Dec; 4(6): S21-3.

Ridker PM, Manson JE, Buring JE, et al: The effect of chronic platelet inhibition with low-dose aspirin on atherosclerotic progression and acute thrombosis: clinical evidence from the Physicians' Health Study. Am Heart J 1991 Dec; 122(6): 1588-92.

Robins SJ, Rubins HB, Faas FH, et al: Insulin resistance and cardiovascular events with low HDL cholesterol: the Veterans Affairs HDL Intervention Trial (VA-HIT). Diabetes Care 2003 May; 26(5): 1513-7.

Singh VN: The role of gas analysis with exercise testing. Prim Care 2001 Mar; 28(1): 159-79 ,vii-viii.

Vittinghoff E, Shlipak MG, Varosy PD, et al: Risk factors and secondary prevention in women with heart disease: the Heart and Estrogen/progestin Replacement Study. Ann Intern Med 2003 Jan 21; 138(2): 81-9.

WOSCOPS Study Group: West of Scotland Coronary Prevention Study: implications for clinical practice. Eur Heart J 1996 Feb; 17(2): 163-4.

Kuczmarski RJ, Flegal KM, Campbell SM, Johnson CL. Increasing prevalence of overweight among US adults. The National Health and Nutrition Examination Surveys, 1960 to 1991. JAMA. 1994 Jul 20;272(3):205–211.

Seidell JC. Obesity in Europe: scaling an epidemic. Int J Obes Relat Metab Disord. 1995 Sep;19 Suppl 3:S1–S4.

Ohlson LO, Larsson B, Svärdsudd K, Welin L, Eriksson H, Wilhelmsen L, Björntorp P, Tibblin G. The influence of body fat distribution on the incidence of diabetes mellitus. 13.5 years of follow-up of the participants in the study of men born in 1913. Diabetes. 1985 Oct;34(10):1055–1058..

Simopoulos AP, Van Itallie TB. Body weight, health, and longevity. Ann Intern Med. 1984 Feb;100(2):285–295.

Stewart AL, Brook RH. Effects of being overweight. Am J Public Health. 1983 Feb;73(2):171–178

Kaplan G, Barell V, Lusky A. Subjective state of health and survival in elderly adults. J Gerontol. 1988 Jul;43(4):S114–S120.

Maddox GL, Douglass EB. Self-assessmentSeidell JC, Bakx KC, Deurenberg P, Burema J, Hautvast JG, Huygen FJ. The relation between overweight and subjective health according to age, social class, slimming behavior and smoking habits in Dutch adults. Am J Public Health. 1986 Dec;76(12):1410–1415.

of health: a longitudinal study of elderly subjects. J Health Soc Behav. 1973 Mar;14(1):87–93

Lifestyle Variables, Non-traditional Cardiovascular Risk Factors, and the Metabolic Syndrome in an Aboriginal Canadian Population
Obesity, March 1, 2006; 14(3): 500 - 508

Abdominal obesity, insulin resistance, and cardiovascular risk in pre-diabetes and type 2 diabetes
Eur. Heart J. Suppl., May 1, 2006; 8(suppl_B): B20 - B25.

Metabolic Syndrome: Connecting and Reconciling Cardiovascular and Diabetes Worlds
J. Am. Coll. Cardiol., March 21, 2006; 47(6): 1093 - 1100

Prevention and Treatment of the Metabolic Syndrome
Angiology, November 1, 2004; 55(6): 589 - 612.

Heart disease risk among metabolically healthy obese men and metabolically unhealthy lean men
Can. Med. Assoc. J., May 10, 2005; 172(10): 1315 - 1316

Epidemiology of Uncontrolled Hypertension in the United States
Circulation, September 13, 2005; 112(11): 1651 - 1662.
Hypertension in Adults Across the Age Spectrum: Current Outcomes and Control in the Community
JAMA, July 27, 2005; 294(4): 466 - 472.

Coronary Calcification, Coronary Disease Risk Factors, C-Reactive Protein, and Atherosclerotic Cardiovascular Disease Events: The St. Francis Heart Study
J. Am. Coll. Cardiol., July 5, 2005; 46(1): 158 - 165.

D. J. Brown Everyday Life for Black American Adults: Stress, Emotions, and Blood Pressure West J Nurs Res, August 1, 2004; 26(5): 499 - 514

V. Franco, S. Oparil, and O. A. Carretero
Hypertensive Therapy: Part I
Circulation, June 22, 2004; 109(24): 2953 - 2958.
N. Cossrow and B. Falkner
Race/Ethnic Issues in Obesity and Obesity-Related Comorbidities
J. Clin. Endocrinol. Metab., June 1, 2004; 89(6): 2590 - 2594.

M. H. Parker
A Review of Cardiovascular Disease and Treatment Differences in Women
Journal of Pharmacy Practice, June 1, 2003; 16(3): 157 - 163.

L. Fontana, T. E. Meyer, S. Klein, and J. O. Holloszy
Long-term calorie restriction is highly effective in reducing the risk for atherosclerosis in humans
PNAS, April 27, 2004; 101(17): 6659 - 6663

J. F Inciardi, K. McMahon, and B. L Sauer
Factors Associated with Uncontrolled Hypertension in an Affluent, Elderly

Population
Ann. Pharmacother., April 1, 2003; 37(4): 485 - 489.

A. M. Borzecki, A. T. Wong, E. C. Hickey, A. S. Ash, and D. R. Berlowitz
Hypertension Control: How Well Are We Doing?
Archives of Internal Medicine, December 8, 2003; 163(22): 2705 - 2711.

L. L. Yan, K. Liu, K. A. Matthews, M. L. Daviglus, T. F. Ferguson, and C. I. Kiefe
Psychosocial Factors and Risk of Hypertension: The Coronary Artery Risk Development in Young Adults (CARDIA) Study
JAMA, October 22, 2003; 290(16): 2138 - 2148

J. C. Dekkers, F. A. Treiber, G. Kapuku, and H. Snieder
Differential Influence of Family History of Hypertension and Premature Myocardial Infarction on Systolic Blood Pressure and Left Ventricular Mass Trajectories in Youth
Pediatrics, June 1, 2003; 111(6): 1387 - 1393.

Writing Group of the PREMIER Collaborative Researc
Effects of Comprehensive Lifestyle Modification on Blood Pressure Control: Main Results of the PREMIER Clinical Trial
JAMA, April 23, 2003; 289(16): 2083 - 2093.

F. J van Lenthe and J. P Mackenbach
Neighbourhood and individual socioeconomic inequalities in smoking: the role of physical neighbourhood stressors
J. Epidemiol. Community Health, August 1, 2006; 60(8): 699 - 705

C. HAGQUIST
Socioeconomic Differences in Smoking Behaviour Among Adolescents: The Role of Academic Orientation
Childhood, November 1, 2000; 7(4): 467 - 478

Y.-M. Song, R. L. Ferrer, S.-i. Cho, J. Sung, S. Ebrahim, and G. Davey Smith
Socioeconomic Status and Cardiovascular Disease Among Men: The Korean National Health Service Prospective Cohort Study
Am J Public Health, January 1, 2006; 96(1): 152 - 159