

Cardiovascular risk factors in sub-Saharan Africa: a review

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ABSTRACT

Ischemic heart disease is increasing dramatically in the Sub-Saharan Africa (SSA), despite an increasing prevalence of risk factors, and some characteristics of the African people that make the African population subject to the effects of major cardiovascular risk factors. The pace and direction of economic development, rates of urbanization, the changes in life expectancy, associated with different pathophysiological factors are causing an increased rate of atherosclerotic disease in these countries. The prevalence of ischemic heart disease in SSA has shown a significant rise in the next two following decades due to the rising prevalence of risk factors, especially hypertension, diabetes, overweight and obesity, physical inactivity, tobacco use and the dyslipidemia, mainly due to an increase in urbanization. Moreover, thanks to new knowledge, it has been pointed out the difference of individual risk factors in the African population and other populations due to genetic differences. It is estimated that age-standardized approach for ischemic heart disease mortality rates will rise by 27% in African men and 25% in women by 2015 and by 70 and 74%, respectively by 2030. More research is needed in Africa to provide evidence for cardiovascular prevention and treatment to mitigate the oncoming epidemic. Health interventions are needed for preventing or reducing the morbidity/mortality and should be addressed to both children and adults, including score of the risk stratification modified, starting early and aggressive therapy, if necessary.

Introduction

Cardiovascular disease (CVD) is a disabling growing epidemic that causes premature death and decreased quality of life. Globally, CVDs, which include coronary heart disease (CHD), strokes, rheumatic heart disease, cardiomyopathy, and other heart diseases, represent the leading cause of death.¹ Recent population studies demonstrate an increasing burden of CVD and related risk factors in sub-Saharan Africa (SSA).² Despite evidence to suggest that CVD-related mortality rates are increasing in the region, it is only

now being recognized as an important public health issue in sub-Saharan Africa, with coronary artery disease shown to rise in incidence in sub-Saharan Africa.^{3,4} Cardiovascular diseases are the main non-communicable conditions in SSA and now 9.2% of total deaths in the African region are caused by CVD,⁵ being the leading cause of death in the population aged over 45.⁶ Cardiovascular diseases account for 7-10% of all adult medical admissions to hospitals in Africa, with heart failure contributing to 3-7%.⁷ When studies on urban and rural populations were analyzed, the prevalence of CVD was found to be higher in the urban than the rural population.^{8,9}

Behavioral risk factors

The important contributors to this transition are the so-called *globalization* of dietary habits and urbanization. Urbanization is the prime driver for nutrition transition and emergence of obesity, the metabolic syndrome and other non-communicable diseases in developing countries, especially SSA. The current average annual growth of the urban population in sub-Saharan Africa is 4.5%. Over the period 1980-2050, the urban population of Africa, as a whole, is expected to increase from 134 million to 1,264,000 million.¹⁰ The rural-to-urban migration in many of the developing countries exposes migrants to urbanized diets and lifestyle. Dietary changes associated with urbanization are related to the fact that rural dwellers tend to be more self-reliant in obtaining food and also tend to eat

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traditional diets that are high in grains, fruit and vegetables, and low in fat. Once they arrive in urban areas, these same people tend to rely more on external forces for sustenance, resulting in a shift from production of their own food to the purchase of processed foods.¹¹ Major dietary changes include a large increase in the consumption of fats, particularly animal fat and added sugar and a decrease in cereal and roughage intake.¹² This involves major changes of the main cardiovascular risk factors between the two areas¹³ (Table 1). There was evidence of a significant increase in edible oil, indicating a major change in diet; dietary changes include a large increase in the consumption of fats, particularly animal fat and added sugar, associated with the decrease in cereal and fiber intake¹⁴ (Figure 1). In fact, recent global figures from the World Health Organization (WHO) indicate that the prevalence of obesity is not just affecting the developed countries, but is also increasing in the developing countries, where over 115 million people suffer from obesity-related problems.¹⁵

Psychosocial factors

Psychosocial factors increase the number of risk factors. Some studies have shown that the number of countries registering, in recent years, a rise in the number of households owning televisions and computers is inversely proportionate to the reduction in physical activities, contributing to the obesity rise in children.^{16,17} Alcohol and tobacco smoking are risk factors towards heart failure, ischemic stroke, heart disease, and acute myocardial infarction.¹⁸ Many studies show how alcohol and tobacco use is related to poverty and low socio-economic positions. Rural areas inhabitants are highly affected by such habits, especially compared to the other risk factors, which are more common in urban areas.^{19,20} Smoking tendency is increasing among men and women in SSA, mainly in the age group between 30 and 49, with particular reference to women, increasing together with ageing.²¹ Furthermore, in many developing countries, psychosocial attitude towards obesity is not seen as a negative factor.^{22,23} Mvo *et al.* and Puoane *et al.* reported

that even if a large percentage of African women were overweight and obese, only a few perceived themselves so.^{24,25} Gambian populations were reported to be more obesity tolerant (acceptance of obese body size as normal) than African-Americans, and much more tolerant than white Americans.²⁶ Moreover, the double burden of under and over-nutrition presents a potentially grave situation, which should deserve more attention from both health and economic agencies engaged in development. While they continue to deal with the problems of infectious disease and under-nutrition, they are experiencing a rapid upsurge in disease risk factors, such as obesity and overweight, especially in urban settings. It is not uncommon to find under-nutrition and obesity existing side-by-side within the same country, the same community and the same household. Children in low and middle-income countries are more vulnerable to inadequate pre-natal, infant and young child nutrition. Simultaneously, they are exposed to high-fat, high-sugar, high-salt, energy-dense, micronutrient-poor foods, which are usually lower in cost but also lower in nutrient quality. These dietary patterns, in conjunction with lower levels of physical activity, result in sharp increases in childhood obesity, while undernutrition issues remain unsolved.²⁷ Recently, the rise of obesity and cardiovascular risk factors were also seen in rural areas of some countries of the developing world. It has to be pointed out that many so-called rural areas are no longer genuinely rural: people are becoming more urbanized even in those areas far from cities. This phenomenon, to some extent, is linked to the so-called *Remittance economy*. Migrant workers remittance led to a relative wealth, even in rural areas influencing some lifestyles.²⁸ Such epidemiological transition is due, in part, to an improved longevity starting from the 1950s, so that more people are exposed to these risk factors, for long enough periods, to cause coronary artery disease (CAD). Globally considering risk factors, it has to be highlighted how the risk-factor burden experienced by blacks differs from that of whites. A recent study conducted in Ghana shows low median levels of cardiovascular risk factors and the prevalence of obesity, hypertension, dysglycemia or diabetes, and dyslipidemia was low too. The preponderance of moderately elevated levels of C-reactive protein was also low. However, the evidence has shown that younger patients (<55 years) were prone to a higher risk of atherosclerotic disease, which decreased ageing.²⁹ Such difference, could be partially explained by the difficult collection of data about the actual incidence of risk factors among African population, which may lie in the complexity of conducting proper surveys in many countries, in order to perform an accurate risk stratification. In addition, women do not smoke or drink publicly, but it can assume that the women exhibit these

Table 1. The main risk factors of urban and rural area.

	Urban	Rural
BMI (kg/m ²)	25.8±6.9	19.3±3.2*
Waist (cm)	85.2±9.9	67.8±9.9*
Waist-hip ratio	0.88±0.09	0.81±0.08*
Triceps skinfold (mm)	17.3±6.8	9.8±5.4*
% overweight (BMI >25)	53.4	5.8*

BMI, body mass index. *P<0.001, age and gender adjusted.

behaviors privately in smaller proportions.³⁰ Moreover there are some pathophysiological peculiarities in the African population, boosting an increased susceptibility to traditional cardiovascular risk factors.

Arterial hypertension

The prevalence of hypertension among urban dwellers in SSA appears to be particularly high, ranging from 8-25 per cent. At the dawn of the twentieth century, high blood pressure was virtually nonexistent among indigenous Kenyans and Ugandans. Starting from 1975, high blood pressure became established in Cameroon, Côte d'Ivoire, Democratic Republic of Congo, Ghana, Kenya, Nigeria, and Uganda.^{31,32} In December 2006, among the adults living in Addis Abeba, the prevalence of hypertension was 50.9% among males and 47.1% among females.³³ In Cameroon the prevalence of hypertension among people aged 15-99 in 2004 was 20.8%, a common issue especially among men.³⁴ In Sub-Saharan Africa, age-adjusted hypertension prevalence and age-specific rates of death from stroke are higher among urban blacks than equivalent white populations.³⁵ Yameogo *et al.* showed resistant hypertension is common in black Africans, and the most affected subjects are people over 60, with limited economic income and living in rural areas.³⁶ Numerous studies have found that such population has an excess prevalence of salt sensitivity, hypervolemia, and low plasma renin activity.^{37,38}

Diabetes mellitus

In 2010, an estimated 12.1 million people with diabetes mellitus (4.2% of the global estimate of 285 million) were living in sub-Saharan Africa.³⁹ The following

year, diabetes prevalence rose to 14.7 million (4.02% of the global 366 million). By year 2030, a 90% projected increase in diabetes prevalence throughout SSA, will skyrocket the number of Africans with diabetes to 28 million.³⁹ The incidence of diabetes mellitus in inherited heart diseases (IHD) remains uncertain because many studies show that, among African population, the main complication of diabetes is the micro-angiopathies compared to Western countries, where the macrovascular complication is the most important.^{40,41} One common pathogenic mechanism for microvascular disease, is rooted in the chemical by-products of reactions between sugars and proteins occurring over the course of days to weeks, producing irreversible protein cross-linked derivatives advanced glycation end (AGE)-product.⁴² The increase in AGE produces growth inhibition and apoptosis of retinal pericytes, also inducing an overproduction of endothelial growth factors, neovascularization, and chronic inflammation.^{43,44} Such actions lead to an increased microthrombosis, capillary blockage, retinal ischemia and the activation of endothelial cells, responsible for important shortcomings involving mesangial cells and stimulating glomerular fibrosis.^{45,46} It has been suggested that, among black population, microvascular damage is due to a different genetic predisposition that stimulates the accumulation of AGEs with all the after-effects.^{45,46} The strong association between diabetes mellitus and hypertension among the African population, compared to the white population, worsens dramatically microvascular damage.^{47,48}

Visceral fat

The phenotype of obesity, found among several ethnic groups in developing countries, appears to be different than among the Caucasian population. Sev-

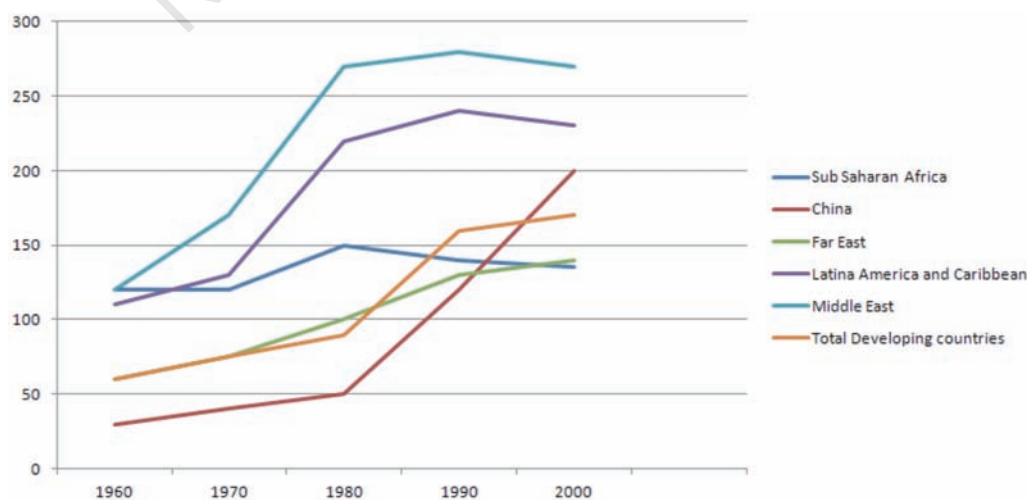


Figure 1. Date of consumption of fats (data from Institute of Medicine, 2010¹⁴).

eral studies reported a correlation between visceral fat (VF) and insulin-resistance, rise of triglycerides, blood pressure and metabolic syndrome. Moreover, VF is correlated to all the conventional cardiovascular disease risk factors and with sedentary life-styles. VF might exhibit a proinflammatory adipokine profile, playing a pivotal role in coronary atherogenesis. The expansion of adipocytes with triglyceride is thought to trigger the increased expression and production of inflammatory cytokines - such as tumor necrosis factor- α , monocyte chemoattractant protein-1, IL-1 β , -6, and -8, plasminogen activator inhibitor-1 and decreased expression and production of leptin and vasoprotective adiponectin. Furthermore, VF might exhibit a proinflammatory adipokine profile^{49,50} (Figure 2). During the International Day for evaluation of abdominal obesity, a study, related to the waist circumference data, involving 63 countries, showed highest prevalence of visceral fat in SSA and South Asians, compared with North Europeans and other Asian ethnic groups.⁵¹ In fact, it was shown that a parity of average value of waist circumference and body mass index (BMI) in SSA, especially Nigeria and Cameroon, visceral adiposity is significantly higher than in other populations.⁵² High percentage of body fat with low BMI value could be partly explained by body build (trunk to leg length ratio and slender body frame), muscularity, adaptation to chronic calorie deprivation,

and ethnicity.⁵³ Some studies have also shown how the populations of SSA have an accumulation of visceral fat in other tissues where usually are not deposited (ectopic fat): this feature has the potential to affect insulin sensitivity.⁵⁴ A number of studies highlighted how African populations have a lower amount of epicardial fat than the white population: such matter is of considerable interest, as the epicardial fat is now considered as an important emerging independent cardiovascular risk factor⁵⁵ (Figure 3). The markers of body fat distribution, including waist-hip ratio, abdominal subcutaneous and visceral fat diner a heritable component, support the thesis of unique genetic variants associated with ectopic fat depots.⁵⁶⁻⁵⁸ Fox *et al.* identified a single nucleotide polymorphisms near the TRIB2 locus, which is associated with pericardial fat but not with body mass index or visceral abdominal fat.⁵⁹ This is the reason why we must carry out studies in order to highlight, among the African population, the genetic variants responsible for the increase in visceral fat but not in epicardial ectopic. This would allow the identification of subgroups among the population, with BMI and amount of visceral fat complying with the standard, who are at greater risk of atherosclerotic disease.⁶⁰ Other factors, such as genotype, could make the African population very susceptible to visceral fat. Among others genetics, a pivotal role is fulfilled by lectin-like oxidized low-density

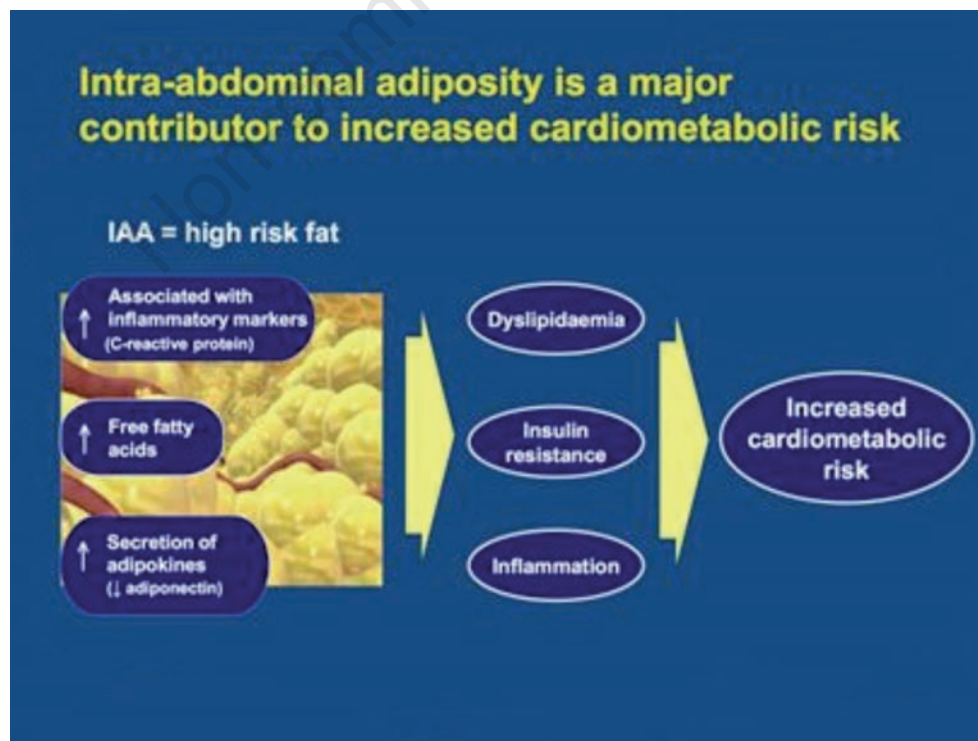


Figure 2. Main mechanisms of cardiovascular damage caused by visceral fat. IAA, intra-abdominal adiposity.

lipoprotein receptor-1 (LOX-1), a type-II membrane protein belonging to the C-type lectin family. The LOX-1 plays a crucial part in amplifying local inflammatory responses during atherosclerotic development⁶¹ (Table 2). The study performed by Predazzi showed a higher frequency of two polymorphisms associated with the risk for CAD and acute myocardial infarction, among the South-Saharan rural populations.⁶¹ Furthermore, it must be considered the identification of other deleterious alleles lying on CVD-associated genes (*GJA4*, *SERPINE1* and *MMP3*), which have a higher frequency in African population compared to Europeans.⁶²

Communicable diseases

Several studies reported associations between the exposure to various infectious agents and the prevalent coronary disease.⁶³⁻⁶⁵ In 1891, Huchard was the first to suggest the involvement of infectious agents in the process of atherosclerosis. Subsequently, several reports shown a relationship between the development of atherosclerosis and the presence of infectious diseases.^{66,67} Several types of microbes are now also being implicated as possible causative agents in acquired CVD, and few bacterial agents have been a research topic for several years. Organisms such as the spirochetes *Borrelia burgdorferi* (Lyme disease) or the *Treponema pallidum* (syphilis), and flagellated bacteria such as the streptococci, have well-recognized atherosclerotic potential. Interest in the role of infection in atherosclerosis was renewed with the observation that patients with coronary artery disease were more likely than matched controls to have an elevated antibody titer to *Chlamydia pneumoniae*.^{68,69} Multiple com-

plex processes are involved in the development of CVD. The increased incidence of infectious diseases has highlighted the expression of proinflammatory immune system to survive up to older ages. Although the increase in the protein c was not related to an increase in atherosclerotic disease, other acute-phase reactants, including fibrinogen and serum amyloid A, appeared to be associated with vascular risk. This selection of a proinflammatory status is confirmed by the higher levels of the proinflammatory cytokine, including the interleukin-6.⁷⁰ The macrophage is a critical component

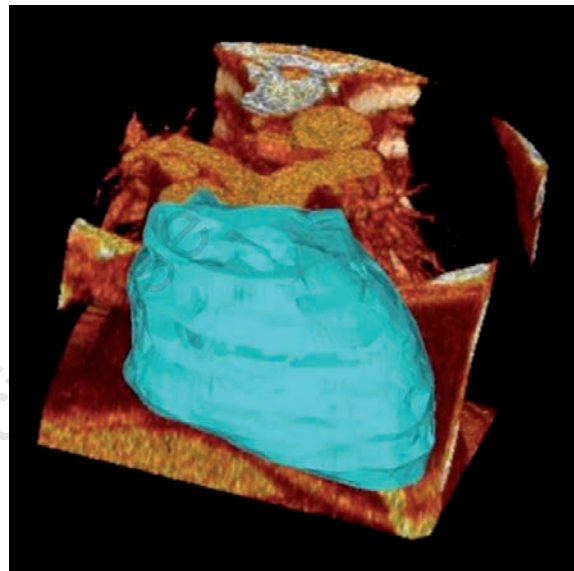


Figure 3. Epicardial fat around the myocardial tissue.

Table 2. Cellular effects of ligand-lectin-like oxidized low-density lipoprotein receptor-1 interaction on atherogenesis.

Endothelial cells alteration of vascular tone
Increased intracellular oxidative stress
Induction of apoptosis
Induction of proliferation and angiogenesis by increasing VEGF expression
Increased expression of adhesion molecules (VCAM-1, ICAM-1, selectins)
Increased expression of monocyte chemoattractant protein-1
Induction of plasminogen activator inhibitor-1
Reduction of endothelial nitric oxide synthase
Release of matrix metalloproteinases
Smooth muscle cells
Induction of apoptosis
Monocytes Induction of monocyte adhesion and activation
Increased oxLDL uptake and foam cell formation

VEGF, vascular endothelial growth factor; VCAM1, vascular cell adhesion molecule-1; ICAM1, intercellular cell adhesion molecule-1; oxLDL, oxidized low density lipoprotein.

in the pathway to atherosclerotic inflammation. During an infectious process causes the activation of macrophages, including the secretion of numerous factors (angiopoietin-related growth factor; transforming growth factor; fibroblast growth factor-1, -2, -4; vascular endothelial growth factor). These substances stimulate the appearance of endothelial cells and are responsible for the creation of a systemic hypercoagulable state.^{71,72} In addition, mitogenic factors are released through an NF- κ B related mechanism, leading to smooth muscle cell proliferation and however there is an increase of monocytes through transendothelial migration at coronary level.^{73,74} This means that the activated macrophages stimulate both local lipid accumulation and the instability that presages plaque rupture.⁷⁵⁻⁷⁷

Coronary heart disease

IHD remains relatively uncommon in SSA despite an increasing prevalence of risk factors but its incidence is rising. A study of the 1954 have been evidenced by 3500 postmortem studies in Ghana in which only three cases of CHD were found.⁷⁸ In Uganda, the National Heart Institute at Mulago alone, currently receives at least 100 patients every day with 5-8 being new cases (a total of about 36,500 patients per year with 1825-2920 being new cases). In 2011, heart cases increased by 20% bringing the number to 12,000 with 256 new cases registered in January alone.⁷⁹ The WHO estimated that in 2005, IHD caused approximately 261,000 deaths in the African region, and current projections suggest that this number will be nearly 600,000 by 2030. It is estimated that age-standardized mortality rates for IHD will rise by 27% in African men and 25% in women by 2015, and by 70 and 74%, respectively by 2030⁸⁰ (Figure 4). The increase in IHD in Sub-Saharan Africa since the 1980s is presumably due to the increasing prevalence among African populations of the classical risk factors for CAD, including hypertension, smoking, diabetes, abdominal obesity and dyslipidemia. In addition, as a re-

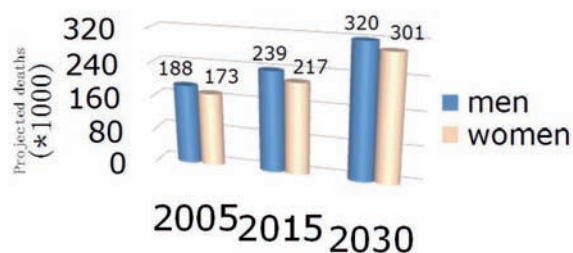


Figure 4. Projection of death from inherited heart diseases in men and women in the WHO African regions for the year 2005, 2015 and 2030 (data from Onen, 2013⁸¹).

sult of developments in combating communicable diseases and a decrease in childhood mortality, life expectancy in Sub-Saharan Africa has risen since the 1950s and the number of individuals aged over 60 is predicted to increase from 39 to 80 million by 2025 in SSA. This means that more people are exposed to these risk factors for long enough periods to cause CAD.⁸¹⁻⁸³

Conclusions

This review attempts to assess the prevalence, levels of risk and major risk factors for developing for cardiovascular disease in SSA. This article answered specific research questions and hypotheses on issues related to sedentary lifestyles, nutritional behaviors, knowledge on CVDs risk factors, and especially some of the key knowledge on the genetic differences between the African population and other populations. Among the socio-economic and behavioral risk profile study variables, the review documented a high prevalence of active smoking, high consumption of edible oil and fat, an increase in physical inactivity and current active alcohol usage. The economic and social important consequences of the CVD Epidemics in the SSA will be devastating. Important gene - environment can play a crucial role in the increased risk of the IHD of the African population. The detection and management of hypertension and diabetes are still unsatisfactory in inner city areas and show variations by ethnic origin. A priority should be the development of scores for the population of Africa, also using the emerging risk factors such as calcium score and visceral fat and considering genetic differences. Increasing burden of obesity, the metabolic syndrome, diabetes mellitus type 2, and CVD in SSA has created an urgent need to strategize mass health policies and intervention programs to tackle nutrition and continuing efforts to manage undernutrition. There are two major approaches to prevention: public health/community-based and clinic-based strategies with a targeted approach to high-risk patients and combinations of these. There are concerns that in comparison with communicable diseases, cardiovascular and relatively chronic diseases have a low priority in the global health agenda and that require this additional emphasis. Finally, we must consider, in the light of the differences between races, strategies for the control of CHD and stroke cushion adopted in European countries directed mostly to white rural populations may be inappropriate for the African population. In conclusion, evaluations must be performed carefully for correct risk stratification, the timing of initiation of treatment and the goals of the therapeutic treatment to be achieved in the African population. In addition, further evaluations should be made to perform correct

public health/community-based strategies targeted at risk factors, including decrease in taxes and prices of fruits and vegetables, more playgrounds, parks, walking and bicycle tracks, provide information to parents about nutrition (particularly mothers), the change of food policy through country-specific guidelines for a healthy nutrition of adults and children.

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