



## Number One Killer: Vascular Disease

Gundu HR Rao\*

Department of Laboratory Medicine and Pathology, University of Minnesota, USA

### Abstract

Heart disease is the number one killer for both males and females. It kills a lot more people than all forms of cancers put together. In fact, it kills more people than all wars or accidents. Cardiovascular Diseases (CVDs) and ischemic heart disease cause more than 40% of all deaths, according to the World Health Organization. These diseases and associated risks, such as hypertension, excess weight, metabolic syndrome, and type-2 diabetes, are called “silent Killers”, as they are not diagnosed till some major symptoms appear, in other words, they are asymptomatic. Because they are asymptomatic, they go unnoticed for long periods of time, and induce subclinical injuries. In 2013, 17.3 million people were killed by CVDs, including heart attacks, stroke, heart failure, blood pressure, and diseases of the arteries. More than one in three adults (92 million), had some form of heart disease in 2014, accounted for one in three deaths, more than all types of cancer and respiratory diseases. Every 40 seconds, someone in the USA dies from CVDs and someone has a stroke. Despite more than seventy years of research by Framingham Heart Study (FHS) group, National Heart, Blood, and Lung Institutes (NHLBI) of National Institutes of Health (NIH), USA, and spending more than 316 billion dollars per year, this public health problem has stubbornly held on to the top ranking number one position, worldwide for over 100 years. By 2030, the number of casualties is expected to increase 36% to 23.6 million per year. In this overview, we will discuss some of the expectations, limitations of the past approaches, and present our view points on possible novel future approaches.

### Introduction

Medical and public health research has revealed over decades, enough information about the causes and prevention of acute vascular events, like heart attacks and stroke, yet every assessment to this day, shows that the deaths due to CVDs are on the rise worldwide [1]. Dr. Elizabeth Nabel, the director of National Institutes of Heart, Lung and Blood Institute at the National Institutes of Health, claimed in a New York Times Editorial (Kolata: Lessons of Heart Disease, The New York Times 2007), “that age-adjusted death rates for heart disease dropped precipitously in the past few decades, and prevention and better treatment are major reasons. She went on to say that in many ways, scientists’ hard won and increasingly detailed understanding of what causes heart disease and what to do for it often goes unknown or ignored [2]. “Similarly, an editorial in Science (1996) proclaimed the “end of heart attacks by the end of century” [3]. The Global Burden of Disease (GBD) study, integrated data on disease incidence, prevalence, and mortality, to provide an up-to-date estimate of CVD burden [1]. They concluded that CVDs remain a major cause of premature death, chronic disability, and health loss for all regions of the world. Socio-Demographic Index (SDI), over the past 25 years, has been associated with dramatic decline in CVD, in regions with very high SDI, but only a gradual decrease or no change in most other regions (GBD). Contrary to the statements we have quoted from New York Times and Science, the researchers of GBD study concluded that, “it is concerning that large reductions in atherosclerotic vascular disease mortality, a crowning achievement of public health, are no longer apparent in many world regions, despite impressive advances in technical capacity for preventing and treating CVD”. Some of the studies have reported decline in CVD related deaths in industrial nations, but conceded that deaths related to diabetes is on the rise, in high income countries [4]. According to the researchers at the Department of Epidemiology, Imperial College London, cardiovascular disease mortality has declined, and diabetes mortality has increased in high-income countries. They estimated potential role of trends in population body mass-index, systolic blood pressure, serum total cholesterol, and smoking in cardio mortality decline in industrialized countries. It is of great concern that in spite of reports of this observed decline in the CVD mortality in industrialized countries; globally the CVD remains a number one killer. It is possible, that the rapid increase in the incidence of hypertension, excess weight, obesity, and type-2 diabetes have added to the all-cause mortality observed worldwide [5-

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#### \*Correspondence:

Gundu HR Rao, Department of Laboratory Medicine and Pathology, University of Minnesota, USA, E-mail: Gundurao9@gmail.com

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14]. A report on the global trends in Cardiovascular Diseases (CVDs), prepared for the Committee (April 13, 2009) on preventing the global epidemic of cardiovascular disease, titled "Meeting the challenges in developing countries", concluded, that chronic diseases dominate in most countries today. Analysis of data from 1940 to present indicates that CVD remains first cause death and disability in middle-income countries, transition economies, as well as high income economies. Projected deaths by cause, also points out that death due to CVDs will remain high for years to come worldwide [1]. The researchers of the third National Health and Nutrition Examination Survey (NHANES-3) reported that more than 99% of the men between the ages of 35 and 74 years have at least one risk factor for developing CVD [5].

Just a brief review of literature indicates, that robust management of modifiable risk factors will indeed, reduce the risk for premature mortality [15,16]. Since I am expressing my view point on this very important topic, I totally agree with this finding. I am a diabetic with all the modifiable risk factors. I have managed all the modifiable risks and escaped the premature mortality. Having said that, I should mention that no large-scale clinical trial has been done, to document the cost and effectiveness of efforts to detect early disease, reduce, reverse, or prevent metabolic diseases. We and others have articulated that all the major metabolic diseases, hypertension, excess weight, obesity, metabolic syndrome, and type-2 diabetes have reached epidemic proportions worldwide [17-19]. According to the experts, meeting the Millennium Development Goals of halting the rate in rise of incidence of any of these metabolic diseases by 2025 is next to nothing. According to Jay Cohn, Professor of Cardiology, University of Minnesota, funding agencies and policy makers should be convinced, that the future of health care should prevent disease, rather than to focus only on better and more expensive methods, to treat disease or its clinical complications. He further emphasizes, that the latter approach threatens to bankrupt health-care budget. Prevention is the only solution to these escalating costs. Henry Blackburn a pioneering cardiovascular epidemiologist, University of Minnesota, wrote in his introductory chapter to my book on CVD, "Applications to cardiovascular health includes the prevention of both individual high risk and overall population high risk that is, dealing with "sick populations as well as sick individuals". The future for prevention of individual high risk lies in targeting these individuals, promoting individual and family health, and education and motivation of health professionals in preventive practice, along with wider provision of preventive services [20].

## Discussion

The World Health Organization (WHO) estimates that over 75% of premature CVD is preventable. The INTERHEART study validated the effect of CVD risk factors including dyslipidemia, smoking, hypertension, diabetes, abdominal obesity (waist/hip ratio), dietary patterns, physical activity, consumption of alcohol, blood Apo lipoproteins (Apo), and psychosocial factors to myocardial infarctions. The researchers concluded that, "Abnormal lipids, smoking, hypertension, diabetes, abdominal obesity, psychological factors, consumption of fruits, vegetables, and alcohol, and regular physical activity account for most of the risk for myocardial infarction worldwide in both the sexes and at all ages in all regions. This finding suggests that approaches to prevention can be based on similar principles worldwide and have the potential to prevent most premature cases of myocardial infarction". In summary, this

seminal study showed that nine easily measured risk factors were associated with more than 90% of the risk of an acute myocardial infarction [15]. These researchers also noted that priorities can differ between geographic regions, because of variations in the prevalence of risk factors and economic circumstances. Indians by and large, have a very high incidence of coronary artery disease compared, to other ethnic groups irrespective of where they live [21-24]. A recent study conducted by researchers from the Department of Global Health and Population, Harvard University, USA; Department of Economics, University of Gottingen, Germany; School of Public Health, University of Witwatersrand, Johannesburg, South Africa; Center for Global Health, King's College, London; and Public Health Foundation of India, identified substantial variation on CVD risk among states and socio demographic groups in India. They were more or less trying, to validate the various risk scores, than trying to find the basic underlying cause for this variation [25]. Cardiovascular disease is the leading cause of death in the United States also [26]. Large disparities in total burden of CVD, persists between the US states, despite improvements in CVD burden. According to the authors of this study, difference in CVD burden is largely attributable to modifiable risk exposures. The largest percentage change occurred in the Districts of Columbia, New Hampshire, and New York. The slowest declines were observed in Oklahoma, Arkansas, and Alabama. The highest CVD DALYs was in Mississippi, followed by Arkansas, Oklahoma, Louisiana, Alabama, Tennessee, Kentucky, West Virginia, South Carolina, and Georgia. What is of great significance in this study is the fact, that it took 25 years for states with the largest burden of CVD, to achieve levels observed among the healthiest states in 1990. The authors of this very important study conclude, "Most CVD burden in the United States is from the atherosclerotic vascular disease, and 80% can be attributed to known causal factors. They also noted significant improvements for all states, but the rate of decline varied widely and was strongly associated with an index of socioeconomic level"; globally, the number of deaths due to CVD increased by 41% between 1990 and 2013, climbing from 12.3 million to 17.3 million deaths. Western Europe and Central Europe are the only two regions, where cardiovascular deaths and death rates have declined. Contrary to these findings, Western sub-Saharan Africa and South Asia have seen increases in CVD related deaths [27]. In the USA, approximately 80% of adults between 20 to 80 years are candidates for prevention.

If everyone received the prevention activity for which they are eligible, myocardial infarction could be reduced by 63% and stroke by 31% according to the researchers of the American Heart Association and American Diabetes Association [28]. There is considerable debate regarding the cost effectiveness of prevention vs. management of the risks or diseases. It is a complex topic and experts present fairly convincing arguments on the cost effectiveness or otherwise of various prevention strategies.

In the absence of a clear-cut proof of concept, to prove the benefits of one or the other approach, let me discuss a population-based study, which was a phenomenal success. In 1972, in the eastern province of Finland-North Karelia, middle aged men were dropping dead of heart attacks, at the highest rates in the world. The Finnish Minister of Health, recognized the public health crisis and appointed a young social science graduate named Pekka Puska, to lead a pilot project. In the ensuing decades, Puska pioneered a strategy that lowered male cardiovascular mortality in a population of 170,000 Fins, by some 80% an unparalleled accomplishment [29-31]. In a mini review like this, it

is hard to discuss the life-long work of Pekka Puska, or to provide what all measures contributed to the success of this project. There are number of criticisms of these studies. In addition, it is hard to pin point exactly what lifestyle changes contributed, to the observed improvement in the health of this population. Is it the drop in the meat consumption? The rise in vegetable and fruit consumption? A rising health awareness? Change from butter to vegetable oils? The North Karelia campaign, had tackled the problem from many directions. When I think of the success of North Karelia, I keep asking one question; can we repeat this success in other regions of the world? In his article which summarizes efforts, Puska concludes, "The experiences and results of the North Karelia Project in Finland support the idea that a well-planned and determined community-based programme can have a major impact on lifestyles and risk factors, and that such a development really leads quite rapidly, to reduce cardiovascular rates in the community. Furthermore, they demonstrated the strength of community-based approach in changing the people's risk factors as well as provide practical experience in organizing such activities".

Even in the Presidential debates these days, one of the leading issues debated is health care, and the associated cost of future healthcare. For instance, one popular component in Hillary Clinton's plan was "focus on prevention: wellness not sickness". Experts from time to time state, that "study after study shows, primary and secondary prevention care, greatly reduces future health care costs, as well as increasing patient's health". Even President Barack Obama has argued, "Too little is spent on prevention and public health". In a perspective in the *N Engl J. Med.* titled, "Does preventive care save money? Health economics and the presidential candidates". Professor Cohen and associates, conclude, "In face of increasing constrained resources, there is a realistic way of achieving better health results: conduct careful analysis to identify evidence-based opportunities for more efficient delivery of health care-whether prevention or treatment and then restructure the system, to create incentives that encourage appropriate delivery of efficient interventions [32,33]". Since we have articulated quite at length about the economic benefits of a preventive strategy, we should also discuss some views about the alternate views expressed by the experts. Economic evaluations of preventive health care tend to conclude, that although preventing the need for treatment can offset some costs from avoidable illness, the overall costs can be substantially higher, because of the number of people who must undergo preventive measures. This is especially true of countries like India and China, with large populations [18,28,34-36]. They also argue that, the prevention strategies do not prevent the ultimate death, but just postpone the ultimate event. Furthermore, as the population ages, which is true of majority of countries, downstream health costs of elderly will sky rocket. In an article reviewing the impact of prevention on reducing the burden CVD, Kahn and associates, state, that "ensuring that individuals receive appropriate preventative measures would, at feasible levels of implementation, substantially reduce the number of myocardial infarctions and strokes, adding as many as 130 million life-years and nearly 150 million quality-adjusted life-years to the U.S. adult population over a 30-year period". They predict that the biggest savings come from controlling the Blood Pressure (BP) of non-diabetics, followed by the control of BP in diabetics, by robust management of pre diabetes (plasma glucose >110 mg/dl), and LDL-cholesterol levels [37].

Sustainable Development Goal (SDG)-3 of the United Nations includes, target 3.4 to reduce premature NCD mortality by a third by

2030 [38]. According to this report, the NCDs are heavily clustered in people with low socioeconomic, and are important cause of medical impoverishment.

Jamison et al. [38] calculated the full-income value of health and concluded that the world is vastly under investing in life-saving research and development of preventive policies and health services. In one of many series of articles by this task force, Bertram and colleagues show, that investments in cardiovascular disease prevention and control, provide a very high economic return [39]. According to these researchers, costs and benefits of providing prevention and treatment of ischemic heart disease and stroke in 20 countries, that span all income levels between 2015 and 2030, provide a glimpse at the economic windfall. World Health Organization's (WHO) "Best Buy" interventions for CVD with 50% coverage in 20 countries, could both achieve the NCD target of reducing mortality by a third, and provide a return on investment ranging from 38 Low Income Countries (LICs) to 102 in High Income Countries (HICs). These interventions use three types of approaches-taxation, regulation or legislation, and information-to address tobacco, harmful use of alcohol, poor dietary quality, and physical activity. For instance, a 50% price increase in cigarette taxes in China would prevent 20 million deaths and generate extra USD 20 billion in revenue, annually for next 50 years.

In a recent article in *Lancet* (2018) on this topic by Nugent and associates, authors write that "although regions and countries differ substantially in their prospects to progress, the broad failure to follow through on commitments made at the 2011 UN high-level meeting and subsequent meetings is nothing short of shameful [38]. The action agenda set out in 2011 is already referred to as a failure. Jamison and associates, in their report on global health say, "That returns on investing health are impressive. Reductions in mortality account for about 11% of recent economic growth in low-income and middle-income countries, as measured in their national income accounts [40]". WHO has identified an essential package of "best buy" clinical interventions for NCD control? For ischemic heart disease, stroke, and type-2 diabetes, the interventions are counseling and multidrug therapy (aspirin, beta blockers, antihypertensive, lipid lowering drugs, angiotensin-converting enzyme inhibitors, and glycaemic control) for people, who have had a heart attack or stroke, and for those at high-risk for a CVD event in the next 10 years. In one of the Taskforce's reports, researchers found that investing USD 120 billion for CVD prevention into the 20 countries with the highest NCD burden would avert 15 million deaths, 8 million incidents of ischemic heart disease, and 13 million incidents of stroke, from 2011 to 2030. CVD currently accounts for nearly half of all NCD deaths every year [39].

This article will be incomplete, if we did not discuss the findings of some major multi-country clinical trials. The seven countries Study, is one of the first major study to investigate diet and lifestyle, along with other risk factors for CVD, across contrasting countries and cultures, and over extended period of time [41,42]. This study was conceived by, Prof Ancel Keys of University of Minnesota, with the main hypothesis that the rate of CVD in populations and individuals would vary in relation to their lifestyle, diet, and serum cholesterol. Informal studies in Italy, Spain, South Africa and Japan were conducted from 1952 to 1956. More formal pilot studies were undertaken, from 1956 to 1957 in Finland, Italy and Greece. The seven country study provided evidence:

1. For the concept of sick and healthy populations.

2. That the major cardiovascular risk factors are universal.
3. For the diet-heart hypothesis.
4. That cardiovascular disease is preventable.
5. That a healthy lifestyle, may promote different aspects of health (<http://www.truehealthinitiative.org>).

In 1978 the National Heart, Lung and Blood Institute of the NIH organized the Bethesda conference on the decline in CHD mortality. In view of the fact that there was a severe lack of data, WHO MONICA project was initiated. To study the trends in determinants for CVD mortality, studies were initiated in 38 populations from 1980 to 1990. According to this review, on a worldwide scale, the seven countries study, the Framingham Heart Study, and the WHO MONICA Project, have contributed most to the development of epidemiology and prevention of cardiovascular diseases [43].

## Conclusion

Cardiovascular disease, has remind the number one cause of death, worldwide for over a century. In addition to the known risk factors, such as smoking, cholesterol, hypertension, and blood glucose, metabolic risks such as oxidative stress, inflammation, subclinical atherosclerosis, excess weight, obesity, and type-2 diabetes also promote the development of vascular diseases, as well as contribute significantly, to the precipitation of acute vascular events like, heart attacks and stroke. Framingham heart studies initiated some seventy years ago, by the prestigious National Institutes of Health, USA, has provided us the valuable information about the modifiable risk factors that promote cardiovascular disease. The World Health Organization estimates, that over 75% of the premature CVD is preventable. Several major multi country clinical trials, have reported a decline in heart disease associated deaths, in the industrialized nations. Looks like CVD-related deaths as well as diabetes related deaths have increased in low-income and middle-income countries. This may be due to socioeconomic as well as ethnicity-based differences. Facts that emerge from a review of these reports are that CVD is a major cause of deaths and if modifiable risks are managed well, premature mortality could be prevented.

According to Global Health Reports, deaths due to CVD have increased by 41% from 1990 to 2013. Although several reports suggest a decline in the CVD mortality, substantial increase in the incidence of metabolic risks such as oxidative stress, work related stress, chronic inflammation, subclinical atherosclerosis, excess weight, obesity and diabetes, add to the CVD burden. These observations lead one to suggest, that there should be immediate action by the global health community for preventive action. Of course, we all know that prevention is better than cure. Having said that, we would like to inform the readers that not all experts agree on this topic; in a lead article in the *N Engl. J. Med.* Professor Cohen and associates discuss this dilemma from a totally different perspective. According to these researchers, economic evaluations of preventive health care tend to conclude, that although preventing the need for treatment can offset some costs from avoidable illness, the overall costs can be substantially higher, because of the number of people who must undergo preventive measures. However, Sustainable Development Goals of the United Nations would like to see that the raise in the incidence of metabolic disease be stopped or reduced by 2030. Whether are not these goals are attainable is a million-dollar question.

World Health Organization has developed “best buy” package

for prevention, which includes three types of approaches-taxation, regulation or legislations, and information-to address tobacco, harmful use of alcohol, poor dietary quality and physical activity. They provide an example of China, and speculate that cigarette taxes in China would prevent 20 million deaths and generate USD 50 billion in revenue annually for next 50 years. Member countries of the United Nations made a commitment in 2011 and developed an agenda for NCD prevention. The action agenda set out in 2011 is already referred to as a failure according, to an article in the journal *Lancet* [39]. Despite these set-backs, the remarkable achievements achieved in Finland by the North Karelia project, support the idea that a well-planned and determined community-based Programme, can have major impact on lifestyle and risk factors. It is worth remembering that prevention of chronic metabolic disease is a time-consuming project. This is best illustrated by the fact that it took 25 years for states with the largest burden of CVD to achieve levels observed among the healthiest states in the USA.

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