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Cardiovascular Diseases and Established Risk Factors in Low- and Middle-income Countries

RAPHAEL BAFFOUR AWUAH¹, ERNEST AFRIFA-ANANE¹ AND CHARLES AGYEMANG^{2*}

¹*Regional Institute for Population Studies, University of Ghana, Accra, Ghana;* ²*Department of Public Health, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands*

1.1 Introduction

Cardiovascular diseases (CVDs) are the leading cause of mortality worldwide, with more deaths from CVDs than from any other cause annually [1]. In 2008, it was estimated that CVDs accounted for over 17 million deaths worldwide from a total of 57 million [1]. The CVD burden varies across different world regions. In high-income countries, CVD-related deaths have declined progressively since the mid-20th century because of successful preventive strategies and improved treatment for acute CVD events [2]. By contrast, in many low- and middle-income countries (LMICs), CVD rates are increasing rapidly, and CVD is already the leading cause of death in many countries [3]. It is estimated that over 80% of deaths attributable to CVDs occur in LMICs, with the occurrence being equally distributed among men and women [1]. Estimates show that LMICs experience 300–600 CVD deaths per 100,000 of the population, which is higher than in most high-income countries [1]. This is an unfortunate paradox because many years of progress in the fight against CVD in most high-income countries is being superseded by the rapidly increasing CVD burden in many LMICs [4].

*E-mail: c.o.agyemang@amc.uva.nl

The total number of CVD deaths (mainly stroke and coronary heart disease (CHD)) increased globally from 14.4 million in 1990 to 17.5 million in 2005. Of these deaths, 7.6 million were attributed to CHD and 5.7 million were attributed to stroke [5]. About 51% of deaths due to stroke and 45% of deaths due to CHD are also attributable to hypertension [6, 7].

The burden of CVD in LMICs is expected to increase further. It is estimated that over 23 million people will die from CVD by 2030 [1, 8] and it will remain the single leading cause of mortality and morbidity [8], more than infectious diseases (including human immunodeficiency virus/AIDS, tuberculosis and malaria), maternal and perinatal conditions, and nutritional disorders combined [9]. The largest increase in terms of percentage will occur in the Eastern Mediterranean region and the largest increase in number of deaths in the South-east Asia region.

The main drivers of the increasing burden of CVD in LMICs are the increasing trends in the prevalence of risk factors such as hypertension, obesity and diabetes. Time trend analyses, for example, indicate that the prevalence of obesity in urban West Africa has more than doubled over the last 15 years [10]. The most important behavioural risk factors of CVD are unhealthy diet, physical inactivity and tobacco use. The effects of unhealthy diet and physical inactivity may lead to hypertension, diabetes, dyslipidaemia, overweight and obesity, and subsequent CVDs. This clearly reflects the changing lifestyles in most LMICs, such as consumption of energy-dense foods and refined sugars complemented by less-energy-demanding jobs, particularly in the urban settings. The changing lifestyle is driven mainly by rapid economic growth coupled with the rapid pace of urbanization in LMICs. It has been suggested that it is the rapid development and resulting changes in the social fabric and physical environment that are accelerating the CVD and other chronic diseases epidemic in LMICs [4]. The potentially devastating effects of this trend are magnified by a detrimental economic impact on households and nations, where poverty can be both a contributing cause and a consequence of CVDs and other chronic diseases [2].

The increasing burden of CVD is occurring at a time when communicable diseases are still highly prevalent, particularly in Africa and South-east Asia, placing a great demand on the overburdened and impoverished healthcare systems in many of these countries.

Below we describe the current burden of the main CVDs (i.e. stroke and CHD) and their main risk factors (i.e. hypertension, diabetes, obesity, smoking, physical inactivity, excessive alcohol consumption) in the last 15 years using data from individual studies and systematic review articles known to the authors. Literature searches were performed using electronic databases (PubMed, PsycINFO and Google Scholar) that reported data on the epidemiology of stroke, CHD, hypertension and diabetes, overweight and obesity, smoking, physical inactivity and alcohol consumption in Africa, Asia, the Middle East, Latin America and the Caribbean. The articles used in this review consist of scholarly papers published between 2000 and 2014.

1.2 The Burden of CVD

Stroke

The prevalence of stroke in LMICs in the period between 2000 and 2014 ranged from 114 per 100,000 people in an urban community in Nigeria [11] to 9300 per 100,000 people in an urban area in China [12]. In rural areas of LMICs, the prevalence of stroke ranged from 243 per 100,000 in South Africa [13] to 6500 per 100,000 in Mexico [12]. The prevalence of stroke varied between different studies for some countries. For example, in Egypt, the prevalence of stroke ranged from 508 per 100,000 [14] to 963 per 100,000 [15]. The incidence of stroke ranged from 25 per 100,000 in Nigeria [16] to 250 per 100,000 in Egypt [17]. The prevalence and incidence of stroke was higher in men than in women.

The estimates indicated that stroke prevalence and mortality rates were 25% greater in LMICs relative to high-income countries [18]. Furthermore, a study of 56 population-based registries worldwide showed that there was a 42% decrease in stroke incidence in high-income countries, whereas LMICs experienced a 100% increase in stroke incidence from 1970 to 2008 [19]. In the absence of any meaningful clinical or public health interventions, it is expected that the incidence of stroke will increase further in LMICs.

Coronary heart disease

CHD, the principal component of CVD, is the leading cause of death in all World Health Organization (WHO) regions of the world except for the African region [20]. CHD is not only a disease of the elderly in high-income countries but also has a major global impact on the economically active population, and is a growing concern for LMICs [21]. Even in sub-Saharan Africa, where CHD was not considered as a major public health concern, it now ranks eighth among the leading causes of death in men and women in the region [22]. More importantly, among people aged >60 years, CHD is already the leading cause of death in men and the second leading cause of death in women in the African region. Mensah's study showed the age-adjusted mortality rate for CHD ranged from 111 per 100,000 in Algeria to 277 per 100,000 in Mauritius in men, and 49 per 100,000 in the Seychelles to 161 per 100,000 in Mauritius among women [22]. Additionally, in China, the age-adjusted death rate from CHD in the period under review was 80–128 per 100,000 for men and 57–98 per 100,000 for women [23]. Furthermore, among men aged 35–64, CHD mortality rates were 64–106 per 100,000 in China [24]. High mortality levels have also been reported in many LMICs. Age-standardized mortality due to CHD was 110 per 100,000 in the Federated States of Micronesia, 125 per 100,000 in Samoa and 181 per 100,000 in Nauru [7]. In Mexico, the age-adjusted mortality due to CHD in the year 2000 was 82 per 100,000 in men and 53 per 100,000 in women [25]. In India, it was estimated that 31.8 million people were living with CHD in 2001 [26].

The age-adjusted prevalence of CHD in Iran was 12.7% [27], 5.5% in Saudi Arabia [28] and 5.9% in Jordan [29]. The rising prevalence of risk factors such as

hypertension and diabetes, as well as the weak and overstretched health systems in most LMICs, will most likely exacerbate the burden of CHD in these regions.

1.3 Risk Factors of CVD

1.3.1 Metabolic risk factors

Hypertension

We considered articles that defined hypertension as a measured blood pressure of >140 mmHg systolic and/or >90 mmHg diastolic or as those receiving anti-hypertensive therapy. The prevalence of hypertension ranged from 6.8% in a rural community in Mexico [30] to 69.9% in an urban study among individuals aged 70 and above in Tanzania [31]. The prevalence in rural areas ranged between 6.8% in Mexico [30] and 42.9% in Brazil [32]. The prevalence of hypertension in urban areas, on the other hand, ranged from 12.3% in Kenya [33] to 69.9% in Tanzania [31]. There was a higher hypertension prevalence among males than among females. There were considerable differences in the prevalence of hypertension in studies conducted in the same country. For example, the prevalence of hypertension ranged from 21.9% [34] to 42.1% [35] in China, from 9.3% [36] to 30.3% [37] in Ethiopia and from 15% [38] to 30.3% [39] in India. The evidence from the studies included in this review suggests that the prevalence of hypertension is comparable to that found in high-income countries. The African region has the highest prevalence rate, 46% of adults aged 25 and above, whereas the Americas have the lowest prevalence, at 35%.

Despite the increasing burden of hypertension in LMICs, a large number of people with hypertension are undiagnosed, untreated and uncontrolled [40]. As of 2008, almost 1 billion people had uncontrolled hypertension worldwide [41]. This means that a large number of people in LMICs will be affected by hypertension-related complications unless major efforts are made to halt or reduce the current rising prevalence of hypertension and its poor control.

Diabetes

With regard to diabetes (type 2), articles were included if they reported the prevalence of the condition, impaired fasting glucose and/or impaired glucose tolerance. The prevalence of diabetes in LMICs was as low as 0.4% in a rural community in Uganda [42] and as high as 26.3% in a study conducted in an urban community in South Africa [43]. Most of the studies reported a higher diabetes prevalence among men compared with women. The prevalence in rural settings ranged between 0.4% in Uganda [42] and 17.5% in Sri Lanka [44]. In the studies that focused on urban communities, the prevalence was from 4.4% in Peru [45] to 26.3% in South Africa [43]. The prevalence of impaired glucose tolerance was from 2.2% in an urban community in Nigeria [46] to 21.6% in Ethiopia [47], while the prevalence of impaired fasting glucose ranged from 1.2% in an urban town in South Africa [48] to 12.1% in a study conducted in a rural community in

Angola [49]. Studies conducted in the same country showed some variation in the prevalence of diabetes. For example, the prevalence of diabetes ranged from 4.3% in rural India [50] to 24.6% in urban India [51].

The review of studies on diabetes in LMICs indicated that the rates are as high as rates observed in high-income countries [52]. The number of individuals with diabetes in LMICs is likely to be even higher than current estimates because of a substantial proportion of people living with diabetes who are undetected [53]. This leads to an increase in diabetes complications (principally nephropathy, retinopathy, neuropathy and small-vessel vasculopathy causing lower extremity amputation). These complications account for much of the social and financial burden of diabetes in LMICs [52]. According to the latest estimates from the International Diabetes Federation, the African region has the highest proportion of undiagnosed type 2 diabetes (63%), and over half a million people in the region died from diabetes-related causes in 2013 [53]. This represents 8.6% of deaths from all causes in adults in the region. Moreover, despite the predominantly urban impact of the epidemic, diabetes is fast becoming a major health problem in rural communities in LMICs [54].

The rising prevalence of diabetes in LMICs is, to a large extent, attributed to rapid globalization and urbanization, with subsequent changes in diet, a reduction in physical activity levels and the adoption of sedentary lifestyles. The diabetes epidemic has increased in line with the worldwide rise in overweight and obesity.

Obesity

The prevalence of overweight and obesity is increasing at an alarming rate in both high-income countries and LMICs throughout the globe. WHO estimates indicate that the undernourished population in the world has declined, whereas the overnourished population has increased significantly [55]. Data from WHO show that, globally, there are more than 1 billion adults who are overweight and 300 million obese people. LMICs have been particularly affected, with obesity rates having increased more than threefold since 1980 in the Pacific Islands, Australasia and China [55]. Overweight and obesity are important risk factors for diabetes, CVD, cancer and premature death. In a review of CHD among LMICs, Gaziano *et al.* found a high population attribution factor of 10 and 5%, respectively, for Eastern Asia and Pacific and South Asia and 8% for sub-Saharan Africa [25]. In addition, Kelly *et al.* reported an average prevalence of overweight of 20.4% among women and 16.8% among men for Asian countries compared with those of sub-Saharan Africa, which were 17.5 and 12.1% for women and men, respectively [56]. Although explanations for the high prevalence are complex, it can be attributed to factors such as changes in dietary patterns, low physical activity levels and sedentary behaviours due to increased use of motorized vehicles as urbanization increases [57]. The gender-based prevalence from the studies indicates that women have been more affected by overweight and obesity than men. In India, 30% of females aged 25 and above were considered to be obese compared with 18% of their male counterparts [58]. Urban residents have also been more affected by overweight and obesity compared with rural residents.

For example, in Cameroon, 17.1% versus 5.4% of urban women and men and 3% versus 0.5% of rural women and men, respectively, were found to be obese [59].

As the overweight and obesity epidemic positively correlates with the rising burden of CVD in LMICs, their reduction will have a major impact in reducing the current CVD burden worldwide.

Dyslipidaemia

High cholesterol levels increase the risks of heart disease and stroke [60]. About one-third of CHD is attributable to high cholesterol globally. High cholesterol is estimated to cause 2.6 million deaths and 29.7 million disability-adjusted life years [61]. High cholesterol is a major cause of disease burden in both high-income countries and LMICs as a risk factor for CHD and stroke [62]. In 2008, the global prevalence of high total cholesterol among adults was 39%. The prevalence was higher in women (40%) than in men (37%). In general, raised cholesterol is higher in high-income countries than in LMICs. However, evidence suggests that the levels are increasing in LMICs. The prevalence of high total cholesterol was highest in the WHO European Region (54% for both men and women), followed by the WHO Region of the Americas (48% for both men and women). The WHO African Region and the WHO South-east Asia Region showed the lowest prevalence of high cholesterol (23 and 30%, respectively). Reduction of high cholesterol levels will have a major impact in reducing CHD and stroke in LMICs. It has been found that a 10% reduction in serum cholesterol in men aged 40 and above resulted in a 50% reduction in heart disease within 5 years [63].

1.3.2 Behaviour risk factors

Alcohol consumption

Harmful use of alcohol is an important contributor to the global burden of disease and is the third leading risk factor for premature deaths and disabilities in the world [61]. It is estimated that about 2.5 million people worldwide die of alcohol-related causes every year. Harmful use of alcohol is a major avoidable risk factor for neuropsychiatric disorders and other non-communicable diseases such as CVD, cirrhosis of the liver and various cancers. The prevalence of alcohol consumption is generally higher in males than in females, and in urban residents than in rural residents in LMICs. The proportion of males who regularly consume alcohol is more than twice the number of females (35% versus 13%, respectively) [64, 65].

A considerable scientific knowledge base is available for policy makers on the effectiveness and cost-effectiveness of strategies and interventions to prevent and reduce alcohol-related harm. However, much of the evidence comes from high-income countries and suggests the need for more work on this topic in LMICs. Nevertheless, the current evidence gives sufficient knowledge to inform policy in terms of comparative effectiveness and cost-effectiveness of selected policy measures [66].

Tobacco

Tobacco use is an important risk factor for CVD, cancer and respiratory mortality. Worldwide, 12% of all deaths among adults aged 30 years and over are attributed to tobacco. It kills nearly 6 million people each year [61]. Over 5 million of these deaths are due to direct tobacco use, while more than 600,000 are due to non-smokers being exposed to second-hand smoke. About 80% of the world's 1 billion smokers reside in LMICs. The prevalence of tobacco use ranges from 8.9 to 41.8% [65]. Generally, men in LMICs constitute higher proportions of individuals who use tobacco compared with their female counterparts. This high proportion is among Asian countries such as Nepal and the Federated States of Micronesia compared with sub-Saharan Africa. In the Federated States of Micronesia, one study reported that 37.7% of males compared with 16.7% of females had used tobacco [67]. Knowledge about the health consequences of tobacco use was found to be high among some sub-Saharan African countries like Ghana. In a faith-based study in Ghana, 97% of 167 congregants of some selected churches in Accra had the knowledge that cigarette smoking could cause heart disease and stroke [68].

Considerable progress has been made in global tobacco control since the adoption of the WHO Framework Convention on Tobacco Control. The *WHO Report on the Global Tobacco Epidemic* in 2013 demonstrated that any country can introduce an effective tobacco control programme to reduce tobacco use, irrespective of its political structure or income level [69]. This means that efforts to incorporate all provisions of the WHO Framework Convention into national tobacco control programmes will save more lives in LMICs.

Physical inactivity

Evidence strongly indicates that physical inactivity increases the risk of many adverse health conditions such as CHD, type 2 diabetes and cancers, and also shortens life expectancy. It has been estimated that a 10 or 25% reduction in physical inactivity, for example, could avert 533,000 and more than 1.3 million deaths every year [70]. However, physical inactivity remains a major problem across the world. Globally, 31% of adults aged 15 years and above were insufficiently active in 2008 [1]. In a review by Hallal *et al.*, individuals living in LMICs had lower levels of physical inactivity compared with those living in high-income countries (20% for LMICs compared with more than 40% for high-income countries) [71]. They also found that, in LMICs, there were more individuals who were physically inactive in sub-Saharan Africa compared with those from South-east Asia [71]. Generally, there is an important gender difference in the prevalence of physical inactivity in LMICs. The prevalence of physical inactivity was high among females compared with their male counterparts. For instance, about 88.6% of females compared with 72.6% of males from the Federated States of Micronesia were physically inactive [67]. Similarly, Nepalese females were more physically inactive than their male counterparts (21.9 versus 17.9%). In contrast, Yusuf *et al.* found among four LMICs that higher proportions of males (22.5%) compared with females (17.1%) were physically inactive [65]. Physical

inactivity rates are also relatively high in urban areas compared with rural areas [72]. In Nigeria, physical activity was found to be lower among individuals with a higher income [73]. In addition, neighbourhood safety from traffic and crime at night and during the day were found to be promoters of physical activity [74].

1.4 Implications for the Increasing Burden of CVDs in LMICs

CVDs come with a huge economic burden. Besides the disruption of life functions/activities and loss of life associated with CVD, LMICs face immense economic challenges associated with the epidemic. The costs are twofold: the indirect cost to the national economy (which includes time and productivity loss), and that to individuals and households (which includes income loss of individuals living with CVD and family members, usually the caregivers) [75]. For example, in India, it has been estimated that loss of income of individuals living with CVD and caregivers was 60.5 and 39.5%, respectively [76].

There is also a direct cost to the healthcare system. For example, in China, annual direct costs of CVD are estimated at over US\$40 billion, which is about 4% of its gross national income [77]. In addition, estimated losses to gross domestic product as a result of CVD ranged from US\$20 million dollars in Ethiopia to nearly US\$1 billion in China and India in 2005 [18]. The economic impact is further compounded by the fact that a high proportion of the CVD burden in LMICs occurs earlier among adults in the economically active population [78]. An evaluation of the potential loss due to early onset of CVD in Brazil, India, China, South Africa and Mexico indicated that about 21 million years of future productive life are lost because of CVD each year [79].

Although the economic impact of CVD in LMICs is high, the resources devoted toward healthcare are inadequate. Most LMICs devote about 6% of their gross national income to healthcare compared with 10% in high-income countries [78]. Considering the limited resources available in LMICs, only the interventions that can lead to substantial reductions in the mortality and morbidity of CVD at relatively low cost are likely to be sustainable.

It has been suggested that the prevention of CVD risk factors is a more cost-effective and sustainable approach in dealing with the CVD epidemic in LMICs [80]. Furthermore, paying attention to the prevention and management of CVD risk factors will lower costs of care, foster effective treatment and reduce the burden of CVD, particularly morbidity and mortality [81]. Prevention and management strategies will be more effective if they are structured and integrated [81] (see Koram and Nimako, Chapter 10, this volume). In most LMICs, it is difficult to implement such structured and integrated programmes because of overstretched and poorly resourced health systems and the lack of political commitment or will [82]. To overcome some of these challenges, stakeholders in the health sector in LMICs should draw on the most effective programmes from high-income countries and other LMICs who have managed and reduced the CVD burden in the planning and implementation of CVD intervention programmes [82] (see Koram and Nimako, Chapter 10, and Agyemang *et al.*, Chapter 11, this volume).

1.5 Conclusion

CVDs have increased to approximately 50% of the total disease burden in LMICs undergoing the epidemiological transition. This burden has financial implications for individuals and governments in LMICs. A focus on prevention of CVD may be a more efficient strategy given the limited resources in LMICs. The challenges that LMICs face in the prevention and control of CVD are enormous, including the under-appreciation of the magnitude of the disease burden, poorly resourced healthcare systems for provision of comprehensive preventive and primary healthcare, and increasing urbanization accompanied by the adoption of less healthy lifestyles. Although daunting, these challenges are not insurmountable. Effective intervention programmes or policies will require a multi-disciplinary approach of key national and international players with a strong political commitment.

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