

## REVIEW

# Almanac 2014: Global health and cardiovascular disease\*\*

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**Abstract:** The modern definition of Global Health has expanded its scope beyond neglected diseases and low-income and underdeveloped countries. The current initiatives focus on improvement of health, reduction of disparities and protection against global threats, seeking for interaction with health practices, policies and systems. There has been a growing interest on Global Health research, given the epidemiological transition currently underway in low and mid-income countries and the increasing epidemiological importance of cardiovascular and other non-communicable diseases, to the detriment of infectious diseases and nutritional deficiencies. Various aspects—formerly neglected—of these diseases, such as epidemiology, prevention, diagnosis and therapy, have been addressed in Global Health publications, leading to a better understanding of the importance of health as a public good, beyond borders. Scientific evidence supports broader initiatives in which governments, foundations and the civil society must share responsibilities and funding to achieve health equity, the main goal of Global Health.

## INTRODUCTION

Global Health, formerly referred to as 'International Health',<sup>1</sup> involves numerous aspects of health policies, epidemiology, prevention, diagnosis and therapy for neglected diseases and is not restricted to low resource regions. It is supported by four main bases: (A) clinical decision based on data and evidence; (B) population-based rather than individual focus; (C) social goals; (D) preventive rather than curative care.<sup>2</sup> Broadly, Global Health has been defined as "worldwide improvement of health, reduction of disparities and protection against global threats that disregard national boundaries".<sup>3</sup> The Global Health Education Consortium highlights its relation to "health practices, policies and systems, stressing the differences rather than commonalities between countries".<sup>4</sup> Its mission has been proposed by the US Institute of Medicine as: "fulfilling society's interest in assuring conditions in which people can be healthy".<sup>5</sup> Global Health exceeds the boundaries of infectious or neglected diseases and underdeveloped areas and focuses on multidisciplinary and interdisciplinarity, embraces prevention, seeks equity and emphasises health as a public good, beyond borders.

The aim of this paper was to assess the contribution of 'Heart' to Global Health knowledge related to cardiovascular diseases (CVDs), reviewing articles published in the past 2 years (from May 2012 to April 2014). Given the breadth of important topics, we categorised our review into studies relevant to understanding CVD epidemiological transition, trends in morbidity and mortality, aspects of vascular diseases and non-CVD, cardiovascular manifestations of selected communicable diseases, other CVDs and cardiovascular health promotion.

## EPIDEMIOLOGICAL TRANSITION

In the last century, with the improvement in health conditions, the world has lived a change of the predominant causes of death from infectious diseases and nutritional deficiencies to non-communicable diseases (NCDs), such as cancer, diabetes, respiratory and cardiovascular diseases.<sup>6,7</sup> This 'epidemiological transition' resulted from population aging—due to lower fertility rates and greater life expectancy—and the rising rates of urbanisation that, along with globalisation, favoured health behaviours that raised the burden of cardiovascular risk factors for ischaemic heart disease (IHD) and stroke, the main causes of mortality worldwide.<sup>7</sup>

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Indeed, equations that integrate age, risk factors and health behaviours in a variable defined as 'cardiovascular risk age' have been proposed as practical and intuitive methods for communicating about cardiovascular risk.<sup>8</sup>

Although the epidemiological transition has already occurred in high-income countries (HICs), like the USA and Western Europe, it is happening in different paces in low and middle-income countries (LMICs),<sup>9</sup> commonly affecting individuals at premature ages and from poorer ethnic groups or regions.<sup>9,10</sup> In the Sub-Saharan Africa, for example, CVDs such as rheumatic heart disease and HIV-related disorders are highly prevalent, although hypertensive heart disease and stroke have more recently become established causes of death and disability, resulting from poorly controlled hypertension.<sup>11</sup> Recent WHO STEPwise approach to surveillance (STEPS) surveys suggest that the rates of CVD risk factors are still lower in these countries than other regions of the world—but should not be considered low—although the rates of IHD remain low. In countries where population aging has evolved, such as in South America,<sup>10,12</sup> unhealthy lifestyles became more common, resulting in higher rates of atherosclerotic CVD, that occurs in more premature ages when compared with HIC.<sup>7</sup> The efforts to prevent, diagnose and treat IHD, stroke and their risk factors delay the morbimortality from these diseases, which will then usually occur at ages above 50 years.<sup>7</sup> Data from Nordic countries registries show that despite the aging process, such efforts still result in steep declines in age standardised CVD mortality.<sup>13</sup>

## CURRENT MORBIDITY AND MORTALITY TRENDS

It is estimated that CVDs account for about a third of all deaths worldwide, being also responsible for a great number of disabilities and significant economic impact. In the Americas, a study showed that from 2000 to the present, CVD comprised 33.7% of recorded deaths (with 42.5% attributed to IHD), with higher rates in women.<sup>12</sup> The 20% mortality reduction in the continent during this period has mainly occurred in HICs—around 50–80%—and mortality and hospitalisation rates are decreasing.<sup>14,15</sup> However, discrepancies can be observed across nations and even in regions of the same country,<sup>10</sup> which may reflect inequality in access to healthcare and preventive policies.<sup>9</sup> The median of CVD death rates of American LMICs, for example, is 56.7 higher compared with HICs (Figure

1)<sup>12</sup> and a study conducted in the same time frame in Brazil showed that, although falling, death rates are still higher than those observed in wealthier countries.<sup>10</sup> In China, on the other hand, IHD mortality increased since 1984, driven by persistent smoking, high cholesterol levels and population aging.<sup>9</sup>

## VASCULAR AND NON-VASCULAR DISEASES

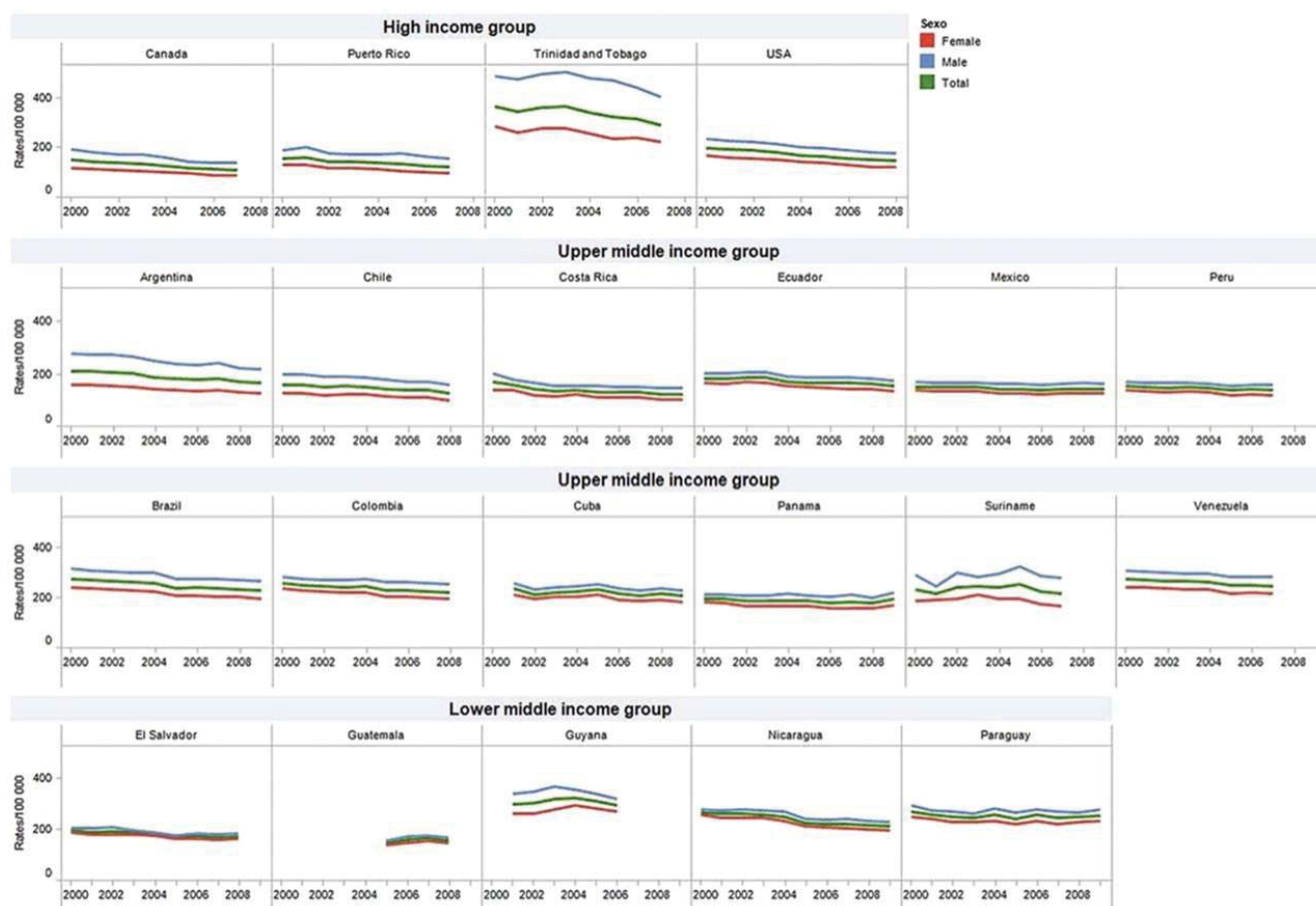
### Health behaviours and risk factors

Most of the CVD burden can be attributed to a small number of lifestyle factors<sup>9</sup>—diet, exercise practices, smoking and alcohol consumption. Among these health behaviours, the regional and social peculiarities of dietary habits are known to have a significant cause-effect relationship with CVD. For example, higher serum concentrations of n-3 polyunsaturated fatty acids, common in Asian diets, contributed to the lower incidence of coronary calcification in Japanese men in a 5-year follow-up cohort.<sup>16</sup> Similarly, in a Danish cohort a negative dose-response trend was observed between tissue concentrations of n-3 polyunsaturated fatty acids and the new onset of atrial fibrillation (AF).<sup>17</sup> The role of higher calcium intake on cardiovascular risk has also been under evaluation. In 1206 patients of the German KAROLA (*Langzeiterfolge der KARDiologischen Anschlussheilbehandlung*) study, after an acute cardiovascular event, higher baseline serum calcium levels were associated with higher risk of all cause (HR=2.39) and cardiovascular (HR=2.76) death at 8 years.<sup>18</sup> Paradoxically, in another large German population-based cohort, higher total and dairy dietary calcium intakes reduced the 11-year risk of myocardial infarction in 23 980 event-free participants, while stroke risk and CVD mortality were not affected.<sup>19</sup> Tailored salt restriction has been established as an evidence-based measure for hypertension, and also in particular situations—such as chronic kidney disease—and specific ethnicities.<sup>20</sup>

Smoking habits have also been given attention in Global Health research. Cultural habits related to smoking seem to have similar deleterious effects, but are still under investigation. In a cross-sectional study in a large Iranian cohort, for example, the association of water-pipe smoking and CVD prevalence was consistently shown (HR=3.75), whereas chewing nass did not have the same effect.<sup>21</sup>

### Environmental factors

Although less established, environmental characteristics must also be discussed in CVD epidemiology ro-



**Figure 1.** Trends in mortality due to cardiovascular diseases (ICD-10 I00–I99) (age-adjusted rates/100 000). Selected countries (upper, upper middle and lower middle income groups) in the Americas, 2000 to latest available year (adapted from de Fatima Marinho de Souza et al<sup>12</sup>).

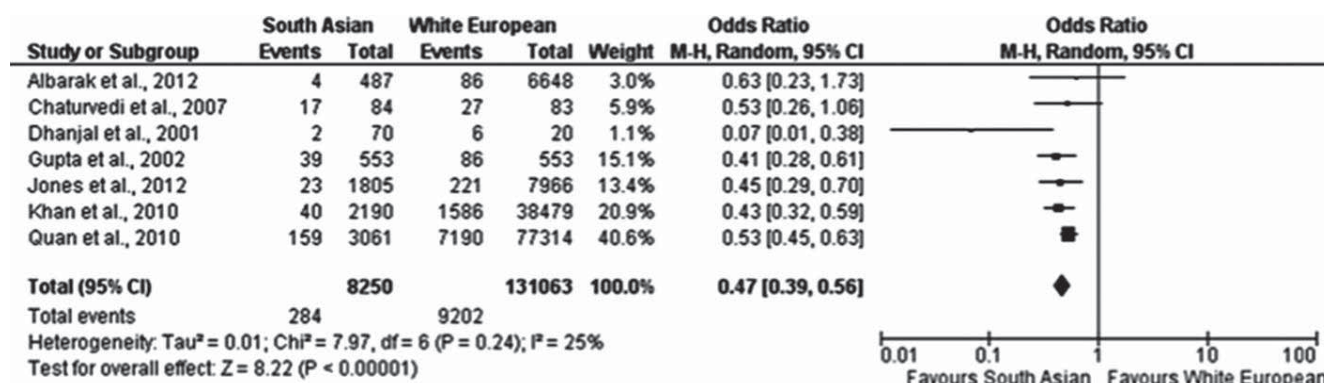
unds. An example is cardiovascular response to extreme temperatures. Cold weather was associated with increased risk of myocardial infarction in different populations and this effect seems to be affected by cultural habits, such as behavioural protection.<sup>22</sup> Epidemiological evidence from a recent surveillance in five Chinese cities demonstrated that extremely hot or cold temperatures increased IHD mortality (18% and 48%, respectively), in a non-linear way.<sup>23</sup> Air pollution is also implied as a trigger for increased all-cause mortality and cardiovascular mortality,<sup>24</sup> with pronounced effects demonstrated in postmenopausal woman.<sup>25</sup> A recent meta-analysis of 29 studies supported that slight increases in particulate matter have an inverse relation with heart rate variability, a marker of worse cardiovascular prognosis.<sup>26</sup> Similarly, exposure to biomass fuel seems to be associated with higher prevalence of carotid plaques (OR=2.6).<sup>27</sup>

### Ethnic factors

The ethnic composition of populations is also implied in differences in CVD burden and outcomes, which

can be attributed to biological, cultural, healthcare and social issues.<sup>28</sup> For example, it has been suggested that Africans and/or Asians might have higher IHD mortality due to intrinsic biological aspects. In Asian Indians, a positive association between high cytomegalo-virus antibodies titres and increased risk of IHD was found, suggesting that infectious disease prevalence may be involved in higher CVD mortality in this population.<sup>29</sup> In the UK, the increased coronary mortality among south Asian minorities was related to a higher incidence of IHD, with similar case fatality.<sup>30</sup> These findings are supported by a meta-analysis that strongly showed that south Asians have higher mortality because of higher incidence of IHD, even though their individual prognosis appeared to be better than that of white populations after adjustment for confounding factors.<sup>31</sup>

This subpopulation also had a higher risk for stroke (OR=1.67) in another British cross-sectional study involving 6292 patients with AF.<sup>32</sup> Paradoxically, in a Canadian cohort involving patients with newly diagnosed hypertension, south Asians had lower risk of death and



**Figure 2.** Forest plot of peripheral artery disease prevalence in coronary artery disease comparison studies, between South Asians and White Europeans (adapted from Sebastiani et al<sup>34</sup>).

adverse cardiovascular outcomes, despite having lower incomes and higher rates of hypertension compared with white patients.<sup>33</sup> Peripheral artery disease prevalence was also significantly lower among South Asians in a meta-analysis of 15 studies (Figure 2).<sup>34</sup> Thus, a combination of metabolic, behavioural and environmental factors are implied in these ethnic particularities, requiring earlier preventive interventions.<sup>30</sup>

Ethnic diversity and its multifactorial mediators may also influence the predictive power of cardiovascular risk scores: neither Framingham nor QRISK performed consistently well in the three ethnic groups evaluated in a primary care Londoner cohort.<sup>35</sup> The understanding of ethnic differences in health is beneficial to minorities and it contributes to decreasing health inequalities in a large sense.

## CARDIOVASCULAR MANIFESTATIONS OF SELECTED COMMUNICABLE DISEASES

Besides IHD, the burden of other CVDs is also different between HICs and LMICs, with the latter dealing with severe cardiac consequences of endemic diseases, typical of their social and economic situation.

In Africa, the impact of HIV infection is considerable, especially in the sub-Saharan region, influencing CVDs. In the Heart of Soweto Study, 10% of patients with newly diagnosed CVD were HIV positive, and the most common HIV-related presentations were cardiomyopathy, pericardial disease and pulmonary hypertension.<sup>36</sup> HIV infection also seems to be associated with sudden cardiac death and its burden is increased by the common association with *Mycobacterium tuberculosis* infection. In HIV-infected patients in sub-Saharan Africa, close to 100% of pericardial effusions are due to tuberculosis; the association with

myopericarditis is common and an important part of it (40%) evolves with decreased LVEF.<sup>37</sup> A factor of major relevance is that HIV-related cardiomyopathy is more common with increased immunosuppression and viraemia, whereas adequate antiretroviral therapy lowers its prevalence,<sup>38</sup> implying that controlling this disease may reduce its CVD consequences.

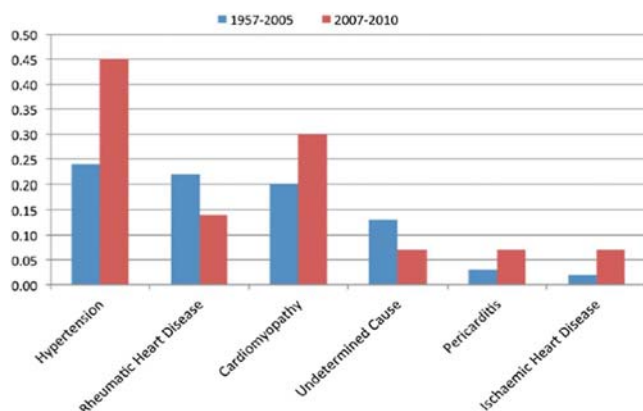
Increased access to medical care and to echocardiography in some parts of the continent has led to the recognition of endomyocardial fibrosis in areas in which the disease had not been previously reported. Although advances in establishing the epidemiology and improving clinical diagnosis and management through medical therapy and improved surgical techniques have been made, unfortunately the mortality related to this disease is still considerable.<sup>39</sup>

## OTHER CARDIOVASCULAR DISEASES

In a review about heart failure (HF) in Africa, it was observed that the main aetiologies that resulted in acute decompensated HF were hypertension, cardiomyopathy and rheumatic heart disease, comprising 90% of cases, a pattern that contrasts with the predominance of IHD in North America and Europe (Figure 3). In this continent, HF affected mainly the young (mean age=52 years), without sex predominance, and is associated with 18% mortality at 6 months, similar to what has been observed in non-African HF registries, suggesting that HF has a dire prognosis independently of the region.<sup>40</sup>

In Tanzania, a study showed that patients hospitalised by HF were younger and their mortality was higher when compared with developed countries. The aetiologies of HF are becoming progressively similar to wealthier countries, with an increase of hypertension and a decrease of rheumatic heart disease.<sup>41</sup> Hyper-





**Figure 3.** Differences in the proportion of causal factors for heart failure in sub-Saharan Africa during the periods 1957–2005 and 2007–2010 (adapted from Sliwa and Mayosi<sup>40</sup>).

tensive cardiomyopathy, once considered rare in sub-Saharan Africa, also seems to be a growing epidemic in this area and, without appropriate control, it will probably result in new patients with HF, and it might increase the incidences of IHD, AF and stroke.<sup>42</sup>

Concerning peripartum cardiomyopathy, a recent South-African study with 176 patients showed that 26% had a poor outcome (death, LVEF <35% or severe symptomatic HF), what translates in great impact, especially if it is considered that this disease affects women in reproductive age. The predictors of worse prognosis were functional class, LVEF and LV end diastolic dimension.<sup>43</sup> A summary of Global Health articles published in *Heart* in the past two years about other non-vascular diseases is in Table 1.

**Table 1. Main Global Health articles published in *Heart* from May 2012 to April 2014 about other non-vascular diseases**

Author/ Year	Country/ Region	Issue	Disease/Factors	Paper type	Study design	N	Main conclusions
Makubi et al, 2014	Tanzania/ Africa	Aetiology and prognosis	HF	Original research	Prospective observational study	427	Patients with HF are younger than in the developed world. Aetiologies are similar—hypertension is becoming more and RHD less important.
Griffiths et al, 2014	UK/Europe	Therapy	HF	Original research	Cost-effectiveness model from a population-based cohort	6505	Ivabradine is likely to be cost-effective in eligible patients with HF in UK.
Syed et al, 2013	South Africa/ Africa	Prognosis	Tuberculous pericarditis and myopericarditis	Original research	Prospective observational study	81	Myopericarditis is common in tuberculous pericardial effusion and associated with HIV-related immunosuppression.
Ogah et al, 2013	Nigeria/ Africa	Epidemiology	HTN	Review paper	Systematic review	N/A	Public health interventions are needed to control the growing HTN epidemic in sub-Saharan Africa.
Mocumbi et al, 2013	Mozambique/ Africa	Epidemiology, prevention and therapy	Endomyocardial fibrosis	Review paper	Literature review	N/A	Joint efforts may be necessary to overcome the lack of expertise and financial constraints for treatment of endomyocardial fibrosis.
Sliwa et al, 2013	South Africa/ Africa	Epidemiology, aetiology and prognosis	HF	Review paper	Literature review	N/A	Improvement of treatment and control of HTN play a central role for the improvement of cardiovascular health in Africa.
Zu'hlke et al, 2013	South Africa/ Africa	Epidemiology, diagnosis and prevention	CHD and RHD	Review paper	Literature review	N/A	Africa still carries a high burden of RHD, and management of simple CHD is yet to be addressed.
Blauwe et al, 2013	South Africa/ Africa	Epidemiology: predictors and outcomes	Peripartum cardiomyopathy	Original research	Prospective cohort study	176	Increased LVESD, lower BMI and lower serum cholesterol are predictors of poor outcome; older age and smaller LVESD are independently associated with a higher chance of LV recovery.
Syed et al, 2013	Nigeria/ Sub-Saharan Africa	Epidemiology	HIV-associated heart disease	Review paper	Literature review	N/A	10% of patients with newly diagnosed cardiovascular disease were HIV+; the most common presentations were HF (38%), pericardial disease (13%) and PAH (8%), with association with immunosuppression and viraemia.

BMI, body mass index; CHD, congenital heart disease; HF, heart failure; HTN, hypertension; LV, left ventricle; LVESD, LV end systolic diameter; N/A, not applicable; PAH, pulmonary artery hypertension; RHD, rheumatic heart disease.

### Box 1. Priority action areas for non-communicable diseases (adapted from Ntsekhe and Damasceno<sup>11</sup>)

Five priority action areas identified at the United Nations High-Level Meeting on Non-Communicable Diseases—September 2011

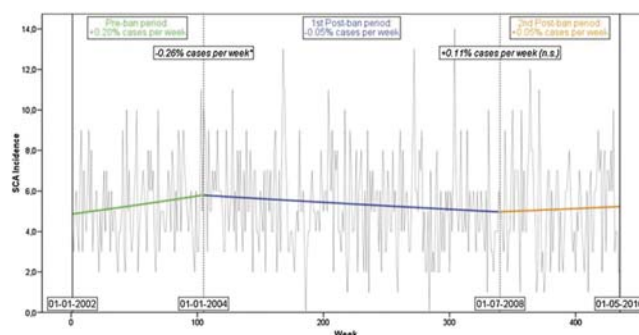
1. Strong committed leadership and political support for a programme action
2. Tackle the priority areas of tobacco control, salt intake, unhealthy diet, alcohol abuse and physical inactivity
3. Increase access and availability of affordable cost-effective treatment
4. Promote local and international partnerships that focus on implementation and research of prevention and control strategies
5. Monitor the determinants and burden of non-communicable diseases, and evaluate progress at global, regional and national levels

## HEALTH PROMOTION, PREVENTION AND CARE OF CARDIOVASCULAR DISEASES

The magnitude of the problem regarding CVD in the current context of Global Health makes facing these diseases a health priority. The challenge faced by HICs is to maintain their achievements in CVD mortality rate reduction conquered in the last decades<sup>9,12</sup> and also to reduce inequities, by promoting this decline in specific minority groups that suffer the greatest burden of CVD in these countries, such as the African Americans in the USA and the South Asians in the UK.<sup>30,44</sup> LMICs live a different reality: CVD mortality rate is increasing in some countries and, although in others it has decreased, the absolute numbers are increasing, mainly due to population aging.<sup>12</sup> Therefore, lessons learned worldwide should be adapted to each country's reality.

To choose where to act, policy makers have evidence revealing that the reduction in IHD mortality rates in HICs are 45–75% a result of risk factor control and 25–55% due to treatment interventions.<sup>6,9</sup> It is clear that policies should focus on population-wide strategies, as well as aim at raising public awareness, empowering people to be partners in their own care; enhancing economic and environmental policies and orientating health systems capacities (Box 1).<sup>11,45,46</sup>

To confront the unhealthy behaviours that lead to the growing incidence of CVD, marketing practices can be used to stimulate physical activity and healthy eating.<sup>6,9,45</sup> Regulating contents of high-energy foods, such as sugary drinks, and subsidising fruits, vegetables and wholefoods can promote healthier diets.<sup>6,9,45</sup> Smoking bans and increased taxation of tobacco and alcohol have been proven to reduce CVD.<sup>6,47</sup> In the Netherlands, the working-place smoking ban significantly decreased the rates of out-of-hospital sudden cardiac deaths



**Figure 4.** Absolute number of observed cases (grey lines) and trends in the incidence (bold lines) of out-of-hospital sudden circulatory arrest between 1 January 2002 (week 1) and 1 May 2010 (week 435). Vertical dotted lines represent the introduction of the two smoking bans, in week 105 (workplace ban) and week 340 (hospitality sector ban), respectively. The text boxes display the slopes (regular font) and changes in slopes (italic) of the unadjusted Poisson regression model. \*Significant change in slope ( $p < 0.05$ ) (adapted from de Korte-de Boer et al<sup>48</sup>).

by about 12% (Figure 4),<sup>48</sup> while in Brazil about 420 000 deaths are estimated to have been prevented due to tobacco reduction over the years 1989–2010.<sup>49</sup>

Improvements in diagnosis and treatment are also important.<sup>9,45</sup> In the Czech Republic, for example, improved case-fatality from 1994 to 2009 had a substantial contribution to the reduction in the national CVD mortality rate.<sup>50</sup> To achieve a greater impact, evidence-based treatments must be: available for all in need, cost-effective and achieve the recommended therapeutic targets.

To be available for all in need, the first obstacle to be transposed is equal access to healthcare. Therefore, the importance of a structured national health systems has gained increasing attention, especially regarding the need for universal coverage, as payment for healthcare can enhance social disparities.<sup>51</sup> Some initiatives have been successful in all world regions, as strengthening primary care and providing free-of-charge medication for chronic diseases.<sup>51</sup> Evidence to suggest that paying for performance—instead of paying for services—improves healthcare is mixed and not yet conclusive, but it's also a promising strategy. Health systems in HICs face the rising costs of technology intensive care for their aging populations and cost-effectiveness studies are essential to optimise allocation of resources.<sup>52,53</sup> LMICs have a more difficult task, as they have to confront the double burden of diseases and the interaction between them, exemplified by the growing numbers of HIV-related CVDs.<sup>7,38</sup> In these countries, health systems must be prepared for the rise of NCDs, but still cope with the burden of communicable and nutritional diseases, to which the social determinants are

even more important, such as the housing conditions for rheumatic heart disease and Chagas heart disease.<sup>11,54</sup> In Africa, regional differences can be seen in the countries' readiness to combat cardiovascular risk factors: 61% had funding available for NCD, however only 26% had a specific policy for diabetes.<sup>55</sup>

To achieve the recommended targets, health workers must be motivated and patients must be adherent, which is a challenge even to structured health systems, such as in the UK, where the majority of patients with IHD or those at high risk of developing CVD do not achieve lifestyle, risk factor and therapeutic targets suggested by the national prevention guidelines.<sup>56,57</sup> Strategies such as the use of telephone calls to monitor adherence are good alternatives to be used.<sup>58</sup>

Another contribution of technology to Global Health is the spreading of information, which may contribute to the implementation of evidence-based interventions worldwide. However, while information travels even to remote areas, the uneven distribution of workforce is still a problem.<sup>59</sup> Sub-Saharan Africa, for example, carries 24% of global disease burden, but has only 3% of health workforce.<sup>40</sup> The poorer and rural areas of the globe have less health workers per 1000 inhabitants, mainly a consequence of poor infrastructure and training.<sup>59</sup> To counteract this trend, technology can also be used for training by online courses and monitoring at a distance, giving the opportunities for shared medical decision. The use of telemedicine for the interpretation of ECGs as a support for primary health in remote areas is a successful example that can be replicated in diverse areas.<sup>60</sup>

In a broader aspect, cooperation is essential if the global community wants to respond to conditions that affect their health. Regarding environmental sustainability, coordinated actions are important to achieve goals such as the reduction of pollution and, consequently climate changes.<sup>23,26</sup> Global Health initiatives should focus on long-term strategies that promote peace, mitigate the impacts of poverty and are in synergy with the needs of the global and local communities.<sup>61</sup> Global commitments to achieve reduction in NCD mortality, such as proposed by the United Nations that aims at a 25% reduction in premature NCD mortality by 2025 (the 25×25 goal) need efforts from local governments and international institutions.<sup>62</sup>

Research and technology development still needs to give more attention to neglected conditions. Diseases that mainly affect LMICs must be in the focus of research institutes worldwide and also be an opportunity for collaboration between countries. Good quality

data about demography, epidemiology and the burden of diseases in this group of countries are also lacking, making identification of weaknesses, planning and implementation of solutions harder in these countries. Surveillance and information sharing is key to make the globe healthier.<sup>62</sup>

## CONCLUSION

The approach to improve Global Health requires the development and implementation of solutions based on information derived from a variety of disciplines including medicine, demography, epidemiology, public health and economy to help policy decision making.<sup>4</sup> Heart manuscripts have advanced significantly in these topics in the past 2 years, contributing to their understanding and dissemination. However, some particular gaps such as health education and effectiveness of screening programmes still need to be addressed in scientific literature.

Trying to benefit from lessons learned across the world and adapting them to local appropriateness, the main objective of Global Health is to emphasise health equity. This task will be achieved by embracing promotion and prevention using population-wide interventions and also through effective delivery of clinical care at the individual level. Governments, foundations and the civil society from countries with different incomes must be willing to share responsibilities and funding in a common perspective, to reach health and well-being of people around the world.

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