Global shifts in cardiovascular disease, the epidemiologic transition and other contributing factors: Towards a new practice of Global Health Cardiology

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Key Words

Epidemiology, demography, health transitions, developing countries, cardiology, global health

Key Points

- Developed countries had more than one century to double or triple their population, whereas the same increases in population size in the developing world occurred just over decades.
- The epidemiological transition theory, far from being perfect, introduced a booster to the understanding of the changing dynamics of epidemiological profiles.
- Changes in population structures and disease profiles, cardiovascular conditions and its associated comorbidities will continue to challenge health care systems.
- A focus on the most populated regions of the world will contribute to protect the large gains in global survival and life expectancy accrued over the last decades.
- From a low- and middle-income country perspective, current challenges provide an opportunity to redefine the agenda of global health cardiology and global cardiovascular research.

Abstract

One of the major drivers of change in the practice of cardiology, in both developed and developing countries, is population change, whose dynamics can be expressed by secular epidemiological and demographic trends, with increasing survival and life expectancy across all age strata. The sole concept of transition, whether epidemiological or demographic, is quite dynamic. From a global health point of view, one element merits attention: developed countries have had longer time to double or triple their population, usually more than one century, whereas the same increases in population size in the developing world occurred just over decades. The epidemiological transition theory, far from being perfect, introduced a booster to the understanding of the changing dynamics of epidemiological profiles and provided a complement to the discourse of the demographic change. In this article, with an special

emphasis on the challenges faced by low- and middle-income settings, we describe current debates of the epidemiological transition paired with other ongoing transitions with direct relevance to cardiovascular conditions. Challenges specific to patterns of risk factors over time; readiness for disease surveillance and meeting global targets; health systems, prevention and treatment efforts; and physiological traits and human-environment interactions are identified. These challenges provide also an opportunity to redefine the agenda of global health cardiology and global cardiovascular research. This article concludes that a focus on the most populated regions of the world, who bear the highest disease burden related to cardiovascular conditions, will contribute substantially to protect the large gains in global survival and life expectancy accrued over the last decades. It then follows that a renewed workforce in global health cardiology must swiftly adapt to these changing environments. As the world changes, the practice of cardiology, clinical cardiology, global health cardiology and cardiology research will follow suit.

Introduction

As the world changes, the practice of cardiology, clinical cardiology, global health cardiology and cardiology research will follow suit. One of the major drivers of change in the practice of cardiology, in both developed and developing countries, is population change, whose dynamics can be expressed by secular epidemiological and demographic trends, with increasing survival and life expectancy across all age strata. These population changes, at the macro level, are not static nor isolated but occur together with many other individual-level changes and adaptations, including but not limited to access to and usage of technological changes [1], changes in healthcare delivery [2,3], in medical training [4], and in the practice of medicine [5], or even changes within the human subject, taking for example changes in height of populations over time [6] as well as changes within individuals as the recently shown link between microbiota and stroke outcomes [7]. In this regard, over the last few years it is becoming more common—and indeed necessary—to encourage interdisciplinary dialogues to better serve medical interventions at the individual- and population-level.

A long trend process of mutual interaction of technologies, policies and social movements, global demographic transition and its epidemiological correlates continue to increase population size across age group, and since the early nineteenth century it has increased by six times. It is projected to further increase up to ten times by the end of this century, by then most countries will endure demographic aging. Life expectancy will continue to grow, doubled in last two centuries, while female fertility will continue to decline. By early nineteenth century, 70% of women's adult life was dedicated to bearing children, which has now dropped by 14%, due to lower fertility and longer and healthier living [8].

Much of the transition in mortality and risk factors for non-communicable diseases, including cardiovascular diseases, has been described in detail elsewhere [9–17], but very few have been addressed to a clinical audience, and in particular what does such transitions mean for low- and middle-income settings. In this article we describe current debates and analyze the pertinence and relevance of the epidemiological transition, paired with the demographic transition and signaling other ongoing transitions with direct relevance to cardiovascular conditions. In doing so, we place an emphasis on the challenges of this transition for low- and middle-income settings undergoing rapidly epidemiologic shifts. Finally, this analysis of trends and context

provides with an entry point to delineate the need for a global health cardiology practice that aligns with the major challenges in the most populated regions of the world, who bears a growing burden of cardiovascular diseases and conditions.

The epidemiological transition—its definition and its place in history

The epidemiological transition theory —or model— was coined in the early '70s by Abdel Omran [18]. Published in a time where development debates were influenced by fears of the so-called “demographic explosion,” in Omran’s view the “key difference between epidemiologic transition and demographic transition theories was that the former unlike the latter allowed for multiple pathways to a low-mortality/low-fertility population regime” [19]. In short, Omran’s theory identified three phases of transition, pestilence and famine, receding pandemics, and degenerative and human created. These phases were later nuanced by Olshansky and Ault who added a fourth stage: delayed degenerative diseases [20] —or “hybristic”, influenced by individual behaviors and lifestyles [21]. In relation to cardiovascular disease, **Table 1** shows the classic stages of the epidemiological transition. More recently, given the predominance and rise in body mass index worldwide [22], some authors propose a fifth stage in the transition, i.e. the age of obesity and inactivity [23,24].

Yet, from a historical point of view, Omran was not the first to link population changes to epidemiologic and mortality patterns. Alternative explanations of the epidemiologic changes in patterns of mortality was described few decades before Omran views came in limelight. Thomas McKeown described secular declines in England’s mortality since the eighteenth century throughout industrialization as a connection with better nutrition and sanitation rather than to medical interventions [25]. Omran thesis, on the other side, was more optimistic about the benefits of technology in the developing world, claiming that mortality decline depended more on developing interventions oriented towards supporting national and international programs of health service provision and environmental control [25]. Subsequent analyses, based on new methods and sources, would reveal some flaws of the McKeown assumptions [26], as has also happened to some of Omran claims, in relation to the double burden or overlapping of both communicable and non-communicable diseases [27].

Importantly from a contextual view, such debates around patterns of mortality took place by the '70s, after the dominance of a discourse around infectious diseases, by then allegedly soon to

be globally controlled, and just some years before emerging and reemerging infectious diseases would recover momentum. In the last two decades the concept of the epidemiological transition has gained even more attention, including its “revisionist” versions [28] stressing the relevance of the concept of societies, particularly for developing countries together with the World Bank, and its approaches in health economics [29], showing concerns about the health of adults and chronic diseases. Far from being a perfect theory to explain transitions, Omran’s epidemiological transition allowed for a conversation in terms of populations and specifically into population’s health. As suggested by others, “an expanded model of transition should account for the immense regional variation in disease burden, disparities in health systems, and the stacking of multiple kinds of epidemics within small areas and over short periods of time” [17].

Not one, but several overlapping transitions

The sole concept of transition, whether demographic or epidemiological, is quite dynamic. From a global health point of view, one element merits attention: developed countries have had longer time to double or triple their population, usually more than one century, whereas the same increases in population size in the developing world just occurred over decades. Whilst most nations accommodate to population growth, other transitions are directly relevant to cardiovascular health. Urbanization, nutrition and diet, food systems [30], culture and technology, interplay one with another to contribute to sustained increased survival in a long-run shift from low to high life expectancy [31].

According to the demographic transition approach, in both the developing and developed world, the longevity transition merits attention [32]. As **Figure 1** shows, the average remaining years to be lived at age 60 will continue to increase, with slight advantage for women compared to men. This longevity transition will have different impacts across heterogeneous societies depending on how they deal with mortality declines and growing morbidity. In so doing, healthcare delivery, its workforce, organization and infrastructure, ethics, economics, and health financing will be directly involved in shaping the future patterns of populations morbidity and mortality.

In the late '80s, Mexican researchers led by Frenk showed that in low- and middle-income countries, alongside the epidemiological transition, there was a transition in the capacity of the the healthcare system to deal with various conditions. In unequal and heterogeneous countries as in Latin America, the paces of epidemiological transition was rather different when compared to developed countries, as simultaneously communicable, poor nutritional and maternal

conditions overlapped with non-communicable diseases, both challenging health systems, a model they called the protracted-prolonged polarized model [33]. To make things even more complex, just one decade before Frenk *et al.*'s analysis, HIV/AIDS entailed a major unforeseen challenge to health systems and health prioritization, particularly for poor countries in sub Saharan Africa.

Cardiovascular disease mortality and risk factors from an low- and middle-income perspective

Much of the transition in terms of cardiovascular disease risk and mortality has been addressed in various reviews published not so long ago [10–15], hence rather than repeating these findings here again, we intend to articulate such trends with other major ongoing societal transitions and current challenges, especially for the practice of global health cardiology. More recently, for disability and mortality-related analyses, newer and more sophisticated methodological approaches have been developed, quantifying the changes in patterns of epidemiological trends as it relates to socio-demographic conditions [34]. Yet, whilst the data are still limited, a different epidemiology of cardiovascular conditions is anticipated for the poorest populations [35]. As foreseen, cardiovascular conditions have played a chief role in driving a global increased mortality, though mostly due to global aging and population growth [11].

From a global health perspective, this scenario has achieved important high-level political pledges to tackle the impact of non-communicable diseases [36], particularly for cardiovascular diseases [37]. More so, recently, cardiovascular premature mortality has been acknowledged as relevant to the recent advances in health and development and has been included in the indicators set of the new Sustainable Development Goals (SDGs), yet its projections for the next decade are not so optimistic [30,38]. Today's environment calls to the global health cardiology and preventive cardiology workforce and practitioners to be well acquainted with broader discourses and understanding the basics of time and place, what transitions have occurred over time and where.

The mortality related to cardiovascular diseases is closely linked to changes over time in the profile of cardiovascular risk factors [22,39–42]. One of the seminal longitudinal studies, the Framingham Heart Study, was launched by the late '40s [43] contributed to the identification of major risk factors for the development of cardiovascular diseases [44,45], such as high cholesterol and elevated blood pressure, today known as common risk factors. In the same vein,

high body mass index has recently been acknowledged as playing a major role in global disease burden in the last decades [46]. Therefore, understanding the patterns of common risk factors over time and across geographical regions is paramount for global health cardiology.

Challenges for global health cardiology

In recent decades, a pattern of decreasing trends in cardiovascular disease mortality has been recorded and studied in high-income regions [10,12]. Yet, the dynamics of such trends are far from being completely known and understood in low- and middle-income countries. The concept of the demographic transition calls for an understanding of the dynamics of changes in population age groups, as populations in general are becoming older. These changes are paired with the co-occurrence of multiple risk factors within the same individual, and within populations, which calls for a rethinking of current approaches to disease burden, especially so when health systems are largely designed for the provision of acute care [47]. For example, shifting an analysis of health patterns centered on mortality to one where the focus is primarily on physical functioning, non-fatal morbidity, or disability. Importantly, morbidity is multidimensional by nature, introducing significant challenges related to health system performance, diagnostic technologies, and even cultural conditions such as the role of caregiving in societies. All of these have indeed multiple implications and new data sources, methods and metrics are to be expanded. In doing so, newer efforts to address these challenges will require reinforced values about data generation and data sharing [48,49], where a direct benefit for low- and middle-income counterparts ought to be affirmed and protected [50].

Low- and middle-income countries carry at least three quarters of the premature mortality due to cardiovascular diseases [51,52]. To address this, international targets have been set, back in 2011, i.e. to reduce the risk of premature non-communicable disease deaths by 25% by 2025 [53]. To address this larger goal, it has to be realized that what works in the developed world might not necessarily work nor should be mechanically implemented in low- and middle-income countries. This has been shown in a series of modeling scenarios pursued for each geographical regions [54]. The latest available report from the World Health Organization on non-communicable diseases signals that only “42 countries had monitoring systems to report on the nine global targets [to achieve 25 by 25]” [55], thus clearly signaling towards substantial gaps in disease surveillance. This, together with the concomitant within-country disparities, are even more evident at the sub-national level. The paucity of data and key information from population-based studies on cardiovascular disease incidence, remission, medical care, and risk or

protective factors [10,11] will somewhat restrain our understanding of cardiovascular disease trends and dynamics in low- and middle-income settings, a major challenge for global health cardiology.

Challenges at the level of health systems are far more complex [56] and ranges from ensuring adequate strategies for primary, secondary, and tertiary prevention [57,58], together with health care delivery services and systems that are affordable, accessible, culturally appropriate and of quality, to legal frameworks and policies. In a world where life expectancy is increasing, how to sustain ideal cardiovascular health across the lifespan [59] and for longer periods over the lifecourse of individuals, and populations, remains pivotal to accrue future larger gains in reducing morbidity and mortality. This is more evident in low- and middle-income countries characterized by contrasting settings with persistent inequality, where poverty will contribute to and impact on demographic and epidemiological transitions [35,60–62]. For example, what primary prevention interventions might work, in the long run, in countries where obesity in early years is increasingly common as in emerging economies or in countries transitioning from low- to middle-income status? In a world where aging and increasing survival are expected to be a major driver of demographic and epidemiological changes, what are the most appropriate approaches to address comorbidity, not only cardiovascular but including other physical and mental chronic conditions? From an economic and development standpoint, acknowledging major underestimations in the costs associated to non-communicable diseases at the household and national levels [63,64], what are the costs of not making major decisions to address avoidable mortality and disability?

Finally, in the area of basic sciences and population health, further areas of interest are related to sex and gender differences in relation to mortality, disability and distribution of risk factors in men and women. Two main drivers usually account for such discrepancies. First, women have longer lifespans in practically all countries, although in some high-income countries such as the United Kingdom this female advantage in life-expectancy is predicted to be reduced in the coming years [65]. Second, women tend to be worse off in receiving care for cardiovascular diseases [66,67], usually linked to more common gender-based discriminations, including access to prevention and treatment. Yet, a third factor that warrants attention for the practice of global health cardiology relates to the physiopathology of heart's aging and its sex differences as a new field or research whose better understanding might suggest avenues to provide better treatment [68]. Besides aging, an important element of women's health agenda directly related to non-communicable diseases is pre-eclampsia, where hypertension, obesity and anemia affect

the health of the mother [69]. In terms of the offspring, one of the outcomes of pre-eclampsia is a restriction of fetal growth, characterized by already well described long term consequences for increased risk of non-communicable diseases, including cardiovascular and metabolic conditions [70–72]. Adding to the complexity offered by low- and middle-income settings, the observed pathophysiologic changes will be compounded with, and will require broader expansions to explicitly assess the human-environment interactions, particularly cardiovascular and metabolic adaptations to high-altitude settings [73–77].

Without extenuating the long list of potential challenges, we have expanded upon Roth *et al.*'s knowledge gaps (**Table 2**) [17], and presented in this section some key aspects in terms of i) patterns of risk factors over time, ii) disease surveillance and meeting global targets, iii) health systems, prevention and treatment efforts, and iv) physiological traits and human-environment interactions. All of them, in addition to challenges to overcome, should be seen as opportunity to redefine the agenda of global health cardiology and global cardiovascular research. As Huffman *et al.* have argued [78], this will also require incorporating additional tools and skills such as implementation science, health systems research, and health policy research.

Unifying global transitions and the practice of Global Health Cardiology—why does this matter?

The impressive attainments in cardiovascular diagnosis and treatment in the last decades in high-income settings cannot overlook the fact that most of them are yet to reach the majority of people living in the global South. Information gaps, such as awareness about actual disease burden and risk factors trends are still present [79], including under-diagnosis and misdiagnosis [80]. Yet, if something was learned from the original conception of the epidemiological transition is that long term trends of change in population's health cannot be overlooked, from larger global and regionals health and development agendas. For example, today's world also host millions of people currently living with HIV, which has now become a chronic condition whose cardiovascular conditions might be neglected [81].

Given that current transition trends will continue its course, the uniqueness of cardiovascular diseases might soon become outdated due to its narrow disease-specific approach when contrasted with individuals living with comorbidities. Therefore, more collaborative, interdisciplinary, and integrative work —as observed with mental health, including the successful models of collaborative care to improve the management of depressive disorders [82–85]— will

be the norm and the demands by patients and by health institutions, both public and private. How can cardiology, and global health cardiology, as a medical specialty prepare for such transition? And, how can health and social protection systems ensure that the increasing demands for cardiology and cardiac rehabilitation are aligned within essential packages of health care provision, with acceptable conditions of quality and dignity? Globally, non-communicable diseases have been linked to substantial impacts at the macroeconomic, health system, and household levels [63,64,86,87], paired with important challenges to inform policy makers in low-income settings about its associated costs [88]. At the household level, stroke is one example of major financial hardship [89]. At the national level, the rise in hypertension in recent years in Mexico is projected to require an increase in financial requirements of 22-24% [90,91], a scenario where additional complexity is introduced if uninsured populations are considered [92]. Availability and affordability of medicines to those who need them has been reported in a large proportion of communities and households across upper middle-income, lower middle-income, and low-income countries [93].

Furthermore, at the country-level, since most of world population are and will remain facing double disease burden, both infectious and noninfectious diseases, how can cardiology reshape and integrate its offerings within current well established clinical practices? Also, a large share of primary prevention, much needed for cardiology outcomes, require interactions with other non-clinical sectors beyond the clinical settings, and cannot be limited to only those now at retirement ages, but to younger generations, as well. All of these scenarios force the new cadre and workforce of global health cardiologists and practitioners to seek beyond the prescription of pharmacological drugs and devices and will force them to incorporate wider radars of practice and skills to inform their avenues for intervention [30,94–96].

From a demographic and long-term perspective, since we are living today in what it is going to be the century of aging, interventions cannot be limited to those who are currently elderly, but also for those that will reach senior years in the coming decades. How can current adolescents and youth be involved in the prevention, and even treatment, of non-communicable diseases? [97,98]. Challenges and opportunities are even greater when focusing cardiovascular prevention efforts in infancy [99,100]. There is strong evidence to support beneficial effects of child obesity prevention programs on body mass index, particularly for programs targeted to children aged six to 12 years [99]. An overview of systematic reviews of population-level interventions that had an environmental component directed to preventing or reducing obesity in children aged 5-18 years showed modest impact of a broad range of environmental strategies on anthropometric

outcomes [100]. Most of unhealthy or protective behaviors and living conditions are initiated and imprinted in these early ages, and today's technology and information revolution could well accommodate to serve as delivery channels to connect and make prevention opportunities available to these population groups.

From a health services perspective, a major challenge is how to continue sharing priorities between communicable and non-communicable diseases [101], while learning from those other countries whose epidemiological profiles have already changed in the last decades. Other challenges include sustaining an adequate political commitment as a source of legitimate concern to mainstream cardiovascular diseases, particularly in the global South [102].

Not surprisingly, cardiology's clinical practice, promotion and prevention, cannot easily be limited or simplistically narrowed only to risk factors at the individual level during a one-to-one short-term clinical encounter. Rather, a minimal understanding of the wider contextual frameworks shaping population's health and health outcomes will enable clinical practitioners to better serve their patients. Such understanding will turn from desirable to essential skills. Consequently, a population health approach is increasingly becoming a core component in the practice of cardiology [103].

The question, then, is not why the practice of cardiology is changing but, on the contrary, what has happened to force and accommodate such change as the norm. This review has signaled major transitions that have occurred in recent decades, with an emphasis placed on low- and middle-income countries. Generational changes, again at the individual- and population-level, have rapidly occurred and become established. One of the obvious examples has been rapidly transitioning from the Barker hypothesis —low birth weight and worse cardiovascular profiles and mortality later in life— to the switch from undernutrition to overweight within a few decades. In the same timeframe, in high-income countries, the benefits of prevention and improved healthcare have been documented, alongside with the known harmful effects of poor access to health care, and income inequalities [104]. Low- and middle-income countries, together with practitioners of global health cardiology, have the opportunity to reshape the anticipated trends of cardiovascular diseases and curb its negative impacts. The demographic transition is introducing large segments of the world's population into ageing. Having accomplished some major successes with the child survival agenda, especially in low- and middle-income settings, these newer adults deserve not to repeat the same fate of mortality described in the original epidemiological transitions. This is why it matters.

Conclusions

The epidemiological transition theory, ever since it was proposed, was an intellectual booster in order to understand the changing dynamics of epidemiological profiles. The epidemiological transition provided a complement to the discourse of demographic change. Despite its criticisms and revisions, it is still an useful concept influencing public health debates, and has proven to be quite influential, particularly in changing societies. Most countries are facing rapidly emerging needs of populations living longer lifespans, with cardiovascular conditions situated at the very core of increasing disease burdens. In these scenarios of changes in population structures and disease profiles, cardiovascular conditions and its associated comorbidities will continue to challenge health care systems. Protecting large gains in global survival and achievements in life expectancy, notoriously accrued over the last decades in low- and middle-income countries, require a broad range of interventions. Fostering encounters and intersections, from human resources to health systems, from individual to population-wide, from health to non-health sectors, and benefiting from technological changes and human rights approaches will provide a solid basis and framework to ensure long-term access to both prevention services as well as health care. A renewed workforce in global health cardiology must swiftly adapt to these changing environments.

Tables

Table 1. Stages of the Epidemiological Transition and its global status, by region

Stage	Description	Life expectancy	Dominant form of CVD	Percentage of deaths attributable to CVD	Percentage of the world's population in this stage	Regions affected
Pestilence and famine	Predominance of malnutrition and infectious diseases	35	RHD cardiomyopathy caused by infection and malnutrition	5–10	11	Sub-Saharan Africa, parts of all regions excluding high-income regions
Receding pandemics	Improved nutrition and public health leads to increase in chronic diseases, hypertension	50	Rheumatic valvular disease, IHD, hemorrhagic stroke	15–35	38	South Asia, southern East Asia and the Pacific parts of Latin America and the Caribbean
Degenerative and human-created	Increased fat and caloric intake, widespread tobacco use, chronic disease deaths exceed mortality from infections and malnutrition	60	IHD, stroke (ischemic and hemorrhagic)	>50	35	Europe and Central Asia, northern East Asia and the Pacific, Latin America and the Caribbean, Middle East and North Africa, and urban parts of most low-income regions (India)
Delayed degenerative diseases	CVD and cancer are leading causes of morbidity and mortality prevention and treatment avoids death and delays onset; age-adjusted CVD declines	70	IHD, stroke (ischemic and hemorrhagic), CHF	<50		High-income countries, parts of Latin America and, the Caribbean

From Gaziano T, Reddy KS, Paccoud F, Horton S, et al., editors. Disease Control Priorities in Developing Countries. 2nd ed. Washington, DC: World Bank; 2011. p. Chapter 33, with permission.

Table 2. Knowledge Gaps and Suggested Next Steps

Gaps in Knowledge	Suggested Next Steps
Mortality data remain absent or of limited quality in some countries, particularly in the poorest regions	<ul style="list-style-type: none"> • Further national investment in sample and comprehensive vital registration systems • Sharing of best practices for data collection and verbal autopsy • Efforts to improve ascertainment of death
Little is known about variation in cardiovascular risk factors and disease burden within some countries	<ul style="list-style-type: none"> • Expansion of household health examination surveys, with wider sharing of results • Broader collection of anthropometric and biomarker data including blood pressure, glycosylated hemoglobin and cholesterol levels • Renewed efforts for population-based surveillance of CVD events, including myocardial infarction and stroke
Changes in cardiovascular mortality are more complex than suggested by a stepwise model of epidemiological transition	<ul style="list-style-type: none"> • National health planning will need to consider a broad range of contextual factors, including local patterns of risk, policies that influence health, and current health system arrangements • Formal CVD costing studies in LMIC to address financial risk and health system efficiencies • Improved cross-cultural measures of disability related to CVD

CVD: cardiovascular disease; LMIC: low- and middle-income countries.

From Roth GA, Huffman MD, Moran AE, et al. Global and regional patterns in cardiovascular mortality from 1990 to 2013. *Circulation*. 2015 Oct 27;132(17):1667–78, with permission.

Figures

Figure 1. Life Expectancy at age 60, selected regions, 1950 – 2100

From United Nations, Department of Economic and Social Affairs, Population Division. World Population Prospects: The 2015 Revision, Key Findings and Advance Tables [Internet]. 2015 [cited 2016 May 4], with permission. Available from:

http://esa.un.org/unpd/wpp/publications/files/key_findings_wpp_2015.pdf

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