Published in final edited form as:
Circ Res. 2014 June 6; 114(12): 1959–1975. doi:10.1161/CIRCRESAHA.114.302782.

Global Perspective on Acute Coronary Syndrome: A Burden on the Young and Poor

Rajesh Vedanthan[1], **Benjamin Seligman**[2], and **Valentin Fuster**[1,3,*]

[1]Zena and Michael A. Weiner Cardiovascular Institute, and Marie-Josée and Henry R. Kravis Center for Cardiovascular Health; Icahn School of Medicine at Mount Sinai; New York, NY, USA

[2]Stanford University School of Medicine and Department of Biology; Stanford, CA, USA

[3]Centro Nacional de Investigaciones Cardiovasculares; Madrid, Spain

Abstract

Ischemic heart disease (IHD) is the greatest single cause of mortality and loss of disability-adjusted life years (DALYs) worldwide, and a substantial portion of this burden falls on low- and middle-income countries (LMICs). Deaths from IHD and acute coronary syndrome (ACS) occur, on average, at younger ages in LMICs than in high-income countries, often at economically productive ages, and likewise frequently affect the poor within LMICs. While data regarding ACS in LMICs are limited, there is a growing literature in this area and the research gaps are being steadily filled. In high-income countries, decades of investigation into the risk factors for ACS and development of behavioral programs, medications, interventional procedures, and guidelines have provided us with the tools to prevent and treat events. Although similar tools can be, and in fact have been, implemented in many LMICs, challenges remain in the development and implementation of cardiovascular health promotion activities across the entire life course, as well as in access to treatment for ACS and IHD. Intersectoral policy initiatives and global coordination are critical elements of ACS and IHD control strategies. Addressing the hurdles and scaling successful health promotion, clinical and policy efforts in LMICs are necessary in order to adequately address the global burden of ACS and IHD.

Keywords

Acute coronary syndrome; epidemiology; global health; low- and middle-income countries; ischemic heart disease

Introduction

Ischemic heart disease (IHD) is the greatest single cause of mortality and loss of disability-adjusted life years (DALYs) worldwide, accounting for roughly seven million deaths and 129 million DALYs annually.[1,2] Cardiovascular disease exerts a significant economic toll,

*Corresponding Author: Valentin Fuster, MD PhD, Icahn School of Medicine at Mount Sinai, One Gustave L. Levy Place, Box 1030, New York, NY 10029, Telephone: 212-241-3799, Fax: 212-423-9488, valentin.fuster@mssm.edu.

Disclosures: None

accounting for one-third of a projected $47 trillion in economic losses to non-communicable diseases (NCDs) over the next 20 years.[3] While high-income countries (HICs) continue to deal with significant IHD mortality, nearly two-thirds of all IHD DALYs and over half of deaths occur in LMICs. Many of these countries have experienced transformational economic growth and lifestyle changes over the past several decades that have increased the prevalence of IHD risk factors and rates of mortality.[4-8] Understanding this change, how it compares with past experience in HICs, and available measures to stem the global tide of IHD mortality make up the research and action frontier regarding acute coronary syndrome (ACS) and IHD in LMICs.

The epidemiologic transition provides a useful framework for understanding the rise of IHD in LMICs (Figure 1).[9,10] The epidemiologic transition posits that populations initially start with low life expectancies with mortality primarily driven by infections, under-nutrition, and illness and injury related to childbirth and early childhood ("age of pestilence and famine"). As sanitation and agriculture improve, these causes of death gradually recede ("age of receding pandemics") until NCDs, particularly IHD and cancers, dominate the causes of death ("age of degenerative and man-made diseases"). Still later, as cancers and IHD become preventable or controllable, the burden of these diseases shift to older ages ("age of delayed degenerative diseases").[11] A "fifth stage" has also been proposed, in light of recent adverse trends in physical activity and diet—an age of "obesity and inactivity".[12]

Rapid urbanization, mechanization of transport, and increasingly sedentary jobs in LMICs have led to an acceleration and overlap between the stages of the epidemiologic transition.[13-16] While infections, under-nutrition, and maternal/child mortality are still important, they are no longer dominant causes of death in many LMICs: IHD is now one of the top five causes of death in all regions of the world except sub-Saharan Africa. Even in sub-Saharan Africa, cardiovascular disease is the leading cause of death among individuals over age 30.[17] Overall, the numbers of deaths and DALYs attributable to IHD have risen since 1990.[18,19] This acceleration in the rise of NCDs without a similar reduction of infectious disease burden, has led to a challenging "double burden of disease" in many countries.[13,20,21] In addition, the age-standardized mortality rates from IHD are higher in many LMICs than in HICs, thus indicating more individuals are dying at a *younger* age from IHD in LMICs (Figure 2).[19] While much of the IHD burden in LMICs is occurring as those regions and individuals enter higher economic strata, there remains a substantial health and economic burden on the poorer segments of LMIC societies resulting from IHD and related NCDs.[22-24] In addition, given population growth in LMICs, the absolute numbers of individuals with premature IHD is substantial even as global, age-standardized IHD mortality rates have declined.[18,19]

There has also been a dramatic rise in several IHD risk factors. Obesity and overweight prevalence has been increasing in many LMICs,[6,25-27] more than tripling between 1975 and 1997 among children in Brazil from 4.1% to 13.9%.[25] The age-standardized prevalence of obesity and overweight increased from 30.8% in 1980 to 46.4% in 2008, with half of the increase occurring after 2000.[27] Globally, mean body mass index has been increasing in nearly every region of the world (Figure 3). Other biological risk factors have demonstrated geographic and temporal variability. Comprehensive analyses of systolic blood pressure

have revealed increases in sub-Saharan Africa and South/Southeast Asia, relatively little change in Latin America, and substantial decreases in HICs (Figure 4).[4] In contrast, mean serum cholesterol levels have tended to decline in several regions of the world, although at varying rates[5]: while HICs and the former Soviet Union have experienced notable declines, South Asia has seen much more modest declines, while Latin America and the Middle East did not change and levels actually rose in East Asia (Figure 5).

Underpinning the rises in biological risk factors have been rises in behavioral risk factors. Though recent reports suggest that global smoking prevalence has declined since 1980, the total number of smokers has increased to nearly one billion people in 2012[28] and remains common in many LMICs[29] despite some notable successes.[30-32] There is also significant geographic variability in smoking rates, with certain areas (Russia, Eastern Europe, Central Asia, China, Southeast Asia, North Africa, and parts of South America) characterized by high age-standardized prevalence of daily smoking (Figure 6). Consumption of other unhealthy products, such as sugary beverages, processed foods, and alcohol have increased.[33] Likewise, large numbers of adults around the world have low levels of physical activity; although there are significant regional variations, several LMICs have physical inactivity levels that rival those of HICs (Figure 7).[34] From the most recent Global Burden of Disease estimates, the top 10 risk factors contributing to mortality and DALYs in LMICs were all behavioral or biological risks for NCDs (Figure 8).[35]

In this review, we aim to describe the global perspective regarding ACS. However, given the limited, though growing, body of data regarding ACS outside of HICs, we use IHD as a surrogate for ACS when data for ACS are not available. Thus, we examine in detail the trends of IHD burden in HICs, compare and contrast the recent experience in LMICs, discuss the history of ACS treatment and prevention in HICs, and outline steps for addressing ACS in LMICs.

Rise and Fall of IHD Mortality in HICs

Current HICs struggled with growing rates of ACS and associated mortality during the mid-twentieth century.[36-38] However, HICs have experienced significant declines mortality rates from all cardiovascular conditions since the 1960s.[39-41] Both treatment and prevention have contributed to the observed reductions in IHD mortality in HICs (Table 1).[42-44] Treatment includes improved care for ACS, as well as chronic medical management of IHD. Preventive efforts include both behavioral and pharmacological initiatives.

Advances in the acute management of ACS include many celebrated achievements in intensive care-related and interventional approaches to cardiovascular medicine: the creation of the coronary care unit[45]; the introduction of streptokinase[46] and later thrombolytic drugs;[47] and the development of coronary artery catheterization, balloon angioplasty,[48] and surgical revascularization.[41,49] These advances made it possible, rather than to simply observe the natural history of ACS complications, to intervene and attempt to modify the natural course of illness. Use of emergency medical systems, initially established for trauma care and to transport patients with suspected ACS, has also helped reduce the time between symptom onset and intervention, despite underutilization by many individuals who have

acute events.[50-52] These interventions have changed acute management from passivity and impotence to activity and intervention, with the potential to avert premature death and disability.

Further success in IHD treatment is reflected in the multi-dimensional approach to medical management of IHD and secondary prevention of further events. This foundation of optimal medical therapy includes a combination of medications that is started acutely and maintained post-ACS: aspirin, beta blockers, angiotensin-converting enzyme (ACE) inhibitors, or angiotensin receptor blockers, and statins. The evidence for their use has been established over several decades, including the ISIS series of trials for beta blockers,[53] aspirin (alongside streptokinase),[54] and ACE inhibitors.[55] Longer-term evidence for these medications has been built up in meta-analyses of numerous trials.[56-59] Evidence for statins began to emerge with low-dose therapies in the 4S and CARE trials,[60,61] while later trials showed the increased benefits of more intensive lipid-lowering.[62-64]

Improvements in primordial and primary prevention were driven first by an understanding of the underlying risks of cardiovascular disease, particularly through the Framingham Heart Study[65,66] and the Seven Countries Study.[67] These and related studies[68] helped define the roles of tobacco use, blood pressure, and cholesterol as risk factors for IHD, challenging beliefs about the benign nature of some risk factors and making what had seemed an inevitable consequence of aging become something that could potentially be prevented.[69,70]

Building on the evidence of risk, intervention studies changed the practice of prevention. Pharmacological intervention was pioneered by the VA Cooperative Studies,[71] showing reductions in morbidity and mortality in individuals treated for hypertension. For cholesterol, the Lipid Research Clinics trial provided early evidence that cholesterol reduction using medication could reduce incidence of IHD.[72] Likewise, dietary and behavior change were first validated with the Oslo Study Group trial,[73] while the North Karelia Project and later the Five Community Study provided evidence of the effects of public health approaches.[74,75] The modern-day guidelines for cholesterol, blood pressure, and lifestyle modification are the result of decades-long efforts to accommodate the latest evidence from rigorous clinical trials into best practice recommendations.[76-80] These efforts, in combination with regulatory initiatives to ban trans fats[81,82] and global tobacco control,[83] have made substantial impact, with corresponding decreases in blood pressure, lipid levels, and tobacco use over time.[84-88]

However, there are still major gaps in the midst of these overall improvements, and also concerning trends with respect to overweight, obesity, and diabetes. Body mass index has increased worldwide virtually without exception.[6] Within the United States, the past decade has seen a rise in the prevalence of obesity among adult men as well as women belonging to racial or ethnic minorities.[89] There have also been declines in physical activity and increases in caloric intake.[90,91] In terms of overall cardiovascular health, less than 1% of adults in the United States were found to have “ideal cardiovascular health”, with high prevalence noted for poor diet (>90%) and high body-mass index (>50%).[92] Projections of these trends suggest that, without intervention, poor health behaviors will continue to be highly prevalent with increases in diabetes prevalence and subsequent cardiovascular complications.[93]

ACS and IHD Burden in LMICs

In some respects, the ACS and IHD situation in LMICs today is more similar to that of HICs in decades past. In particular, the burden of ACS is not solely on the rich nor on the elderly, but also on the poor and working-age[94]. According to the most recent Global Burden of Disease study, the median age of death from IHD among males was a decade younger in LMICs than in HICs in 2010 (Figure 9). This may be due to earlier onset of ACS and IHD, as well as shorter survival after ACS. The available results from the OASIS-1 and -2 registries[95] and epidemiologic studies in India[96-98] suggest that earlier age for first ACS in LMICs is a major contributing factor. Registry data from many other LMICs also support the assertion that ACS often occur at younger ages than in HICs:[99-109] Strikingly, a registry from the United Arab Emirates reported a mean age of 50.8 years.[110] Earlier age for first ACS is likely due to earlier acquisition of adverse health behaviors and IHD risk factors[10,97,111,112] in the current context of economic development and globalization. One notable exception to this overall trend is the experience of an ACS registry in Thailand.[113,114]

The treatment and outcomes of ACS in LMICs are variable but often suboptimal (Table 2).[115] Observational studies do suggest that, to a large extent, the in-hospital treatment of ACS in LMICs includes the use of aspirin, ACE inhibitors, and beta blockers.[95,98,116-118] The ACCESS Study, a prospective observational registry of patients hospitalized for ACS between 2007 and 2008 in 19 LMICs, found that aspirin and lipid-lowering therapies were each given to more than 90% of patients, while uptake of beta-blockers and ACE inhibitors were at 78% and 68%, respectively.[116] However, comparison of countries participating in the OASIS registries found lower use of heparin in LMICs than in HICs, while the ACCESS investigators found that only 39% of patients presenting with ST-elevation myocardial infarction received fibrinolysis. In addition, there also exist substantive within-country differences in the management of ACS, as is the case in India.[115]

Further, continuation of these medications following discharge is poor: investigators from the PURE study found that among individuals with previous cardiovascular events, nearly 70% of those in lower-middle-income countries and 80% of those in low-income countries were on no medication for secondary prevention.[119] They also found lower uptake of lifestyle changes following cardiovascular events in LMICs than in HICs, with 75% of individuals in HICs quitting smoking versus 42% in lower-middle- and 38% in low-income countries.[120] Likewise, the WHO PREMISE survey of coronary artery disease patients in LMICs found that while aspirin was in widespread use and that over 75% of respondents were aware of behavioral risk factors for cardiovascular disease, a majority engaged in less than 30 minutes of physical activity weekly and less than a third were taking statins.[121] Administrative data among IHD patients from Andhra Pradesh were similarly discouraging, with only 15.6% receiving aspirin and 6.0% on cholesterol-lowering medications.[105] Evidence for the quality of clinical outcomes is conflicting. The OASIS registries found comparable mortality rates across participating countries after age-adjustment. By contrast, a review of randomized trials of ST-elevation myocardial infarction treatments found that trial sites in LMICs had higher mortality rates than their counterparts in HICs, which the authors

explained by increased numbers of high-risk patients.[122] Further clarification of the quality of ACS outcomes in LMICs is needed.

In addition, the impact of ACS and IHD on household livelihood is substantial in LMICs. As noted above, in LMICs these events occur at younger ages, often during peak economic productivity. Households experience a double burden both from the great expense of treating ACS and from the loss of income of the affected individual. In general, NCD expenditures increased as a proportion of out-of-pocket health care costs in India from 1995 to 2004, and were found to have greater odds of carrying catastrophic health expenditure than did communicable diseases among hospitalized patients.[123] Additional work confirms that individuals with NCDs have higher health expenditures than individuals with communicable diseases[24,124] and that households with an individual with an NCD are more likely to face catastrophic health expenditures.[124,125] In a multi-country survey of individuals hospitalized for cardiovascular conditions, more than half of the hospitalized individuals reported catastrophic health expenditures or distress financing.[23] Survival with disability, such as diminished exercise capacity that may arise from heart failure related to IHD, may further burden households' stretched finances. Testimonies from individuals living with NCDs are notable for their desire not to be a burden on their families.[126]

The socio-economic gradient of ACS in LMICs is also quite striking. Even in low-income countries, these are diseases that inflict a large burden on the poor. For instance, in South Africa, poorer districts of Cape Town had higher rates of mortality from NCDs than did wealthier districts.[127] In the SAGE surveys of health in six middle-income countries, hypertension prevalence was high, between 30% and 36%, across all income strata.[128] A survey of 1600 rural villages in India found higher prevalence of tobacco and alcohol use and lower intake of fruits and vegetables among poorer respondents.[129] Likewise, more than 70% of individuals with suspected myocardial infarction in the Indian CREATE registry were classified as "poor" or "lower middle income".[130] Further, higher socio-economic status was found to be protective against risk of myocardial infarction in India.[131] While there are likely geographic variations—the poor of sub-Saharan Africa face considerable burden from infectious and nutritional diseases—it is clear that the poor in LMICs do indeed experience a substantial burden of ACS and IHD.

Stemming the Tide: Cardiovascular Health Promotion Throughout the Life Course

Despite the challenges of addressing ACS in LMICs, the time is now to implement interventions aimed at cardiovascular health promotion throughout the life course.[132,133] Health promotion activities directed at all ages, access to essential medicines,[134] improved quality of health care services to manage risk factors and treat acute events, and intersectoral policy initiatives[135] can, in combination, prevent millions of premature deaths in the coming decades. A wide array of interventions are cost-effective and scalable in LMICs[136], and an analysis by the World Health Organization (WHO) of intervention packages for specific risk factors suggests that implementation can be done at very low cost per-person.[137]

There is increasing evidence that IHD risk factors have their origins in early childhood.[138-143] Health promotion interventions targeted at young children may have beneficial impacts both on short-term health behaviors, as well as long-term risk factors.[144-149] Effective school-based interventions are those that include the family, and that center on realistic intermediate objectives such as changes in attitude, knowledge, dietary patterns or levels of physical activity, as early control measures that improve cardiovascular health.[150] Critical to the success of these interventions is community engagement, cultural relevance and appropriateness, optimization of the school environment, and involvement of the family.[151-153] Programs that have been implemented successfully in LMICs[144,145] can be reproduced in other low-resource settings.[154,155]

Addressing dietary risk factors can be cost-effective. An analysis of salt-reduction measures estimated conservatively that a 15% reduction in salt intake could save 2.4 million lives over 10 years at a cost of $0.50 per person,[156] in line with other findings suggesting that salt reduction at processing stages of food production can be cost-effective.[157] Likewise, reductions in saturated and trans-fats by controlling use in food processing can be cost-effective, estimated at $40 per DALY in Latin America when focusing on trans-fats.[136,157] By focusing on processing sources, these interventions are readily scalable, costing less than $0.01 per person.[137]

Physical activity remains a challenge to evaluate; however, the WHO estimates that a public awareness campaign could be implemented at $0.038 per person. One major challenge to physical activity has been urbanization, which has produced mechanized transportation environments that discourage physical activity.[158] However, there are clear interventions for addressing lifestyle and the built environment,[159] and WHO guidelines on physical activity provide a clear way forward.[160] Efforts in Brazil and Colombia to improve physical activity in cities are one example of success in this area,[161] although there is substantial room to improve policies promoting healthy diets and physical activity.[162]

Effective interventions are also well known to reduce tobacco use, many of which are provisions of the Framework Convention on Tobacco Control: restrictions on advertising, packaging, marketing to minors, use in public spaces, and taxes.[83] Extensive analysis has suggested that these interventions produce robust results, with particularly strong response to taxation in developing countries.[163] Further, these are highly cost-effective, from $3-$42 for a 33% tax rate on tobacco to $55-$761per DALY in LMICs for nicotine replacement therapy.[164] The WHO's "best buys" for global health estimate that a package of interventions including taxation, packaging and advertising restrictions, counter-advertising, and use restrictions could be implemented for approximately $0.11 per person.[137] However, there have been several challenges to ratification and implementation of the Framework Convention.[165] One major challenge has been the push for voluntary, nation-level approaches rather than a coordinated global treaty.[166-170] After passage of the Framework Convention, it has been documented that the tobacco industry has attempted to undermine this treaty by subverting its provisions,[171-173] has pursued lawsuits against signatories that have implemented treaty provisions,[174] and has been noted by the WHO as actively preventing implementation of treaty provisions that aim to keep the tobacco industry out of

public health policy-making.[175] Robust and transparent governance is necessary to overcome these challenges.[176]

Treatment of ACS and IHD

Approaches to treatment can be divided into two categories: interventions for acute events and interventions for primary and secondary prevention. According to the Disease Control Priorities Project,[17] streptokinase was the most cost-effective reperfusion therapy at cost $634-$734 per DALY. This strategy, however, became more expensive per DALY saved as time to treatment increased. Alteplase and coronary artery bypass surgery were both over $10,000 per DALY. The use of aspirin, beta blockers, and ACE inhibitors was found to be cost-effective, and in some circumstances cost-saving. To date, there remains a dearth of research on the cost-effectiveness of reperfusion therapies in LMICs.[136] In-hospital use of other evidence-based management, such as anticoagulation, antiplatelet medications, and statins, can be improved with the implementation of systems-level approaches such as reminder, checklists, case management, and educational materials.[177]

For primary and secondary prevention, a multidrug regimen consisting of a beta-blocker or calcium channel-blocker, an ACE-inhibitor, aspirin, and a statin was found to be cost-effective.[178] On the basis of the need for a multidrug regimen for pharmacotherapy, efforts have been made at creating a polypill that brings together these various medications and makes adherence simpler.[179-182] A meta-analysis of trials found that, compared to placebo, a polypill did reduce blood pressure and serum lipids.[183] The polypill strategy is generally thought to be associated with improved adherence related to fewer number of pills to be consumed on a daily basis. However, the data regarding adherence of a cardiovascular polypill are mixed. The meta-analysis concluded that the polypill strategy had lower rates of adherence, with 20% of polypill recipients discontinuing use versus 14% of those on placebo or monotherapy, although the trials included were highly heterogenous.[183] On the other hand, the more recent UMPIRE study found much higher rates of adherence for those receiving a polypill versus usual care.[184] If the challenges in developing a polypill are overcome, it is possible that this, too, will be a cost-effective and essential tool for prevention.[185,186]

Medication access remains a significant challenge in LMICs.[187,188] Data from India indicate that poor patients are less likely to receive evidence-based in-hospital treatments such as revascularization, thrombolytics, and lipid-lowering drugs.[130] Surveys of medication use suggest low levels of uptake of therapy for primary and secondary prevention of IHD.[119,121] Affordability is an important reason as to why uptake is so low: IHD medication may cost more than an individual's daily income.[24,136] As these medications must be taken daily for many years, cost is a primary concern in ensuring that the majority of those in need have the ability to access appropriate care. Innovative strategies to optimize the health care workforce to manage IHD and ACS,[189] as well as to improve access to essential medicines,[134] are required.

Integrated Health Service Delivery, Intersectoral Policy, and Global Coordination

Health care delivery systems in LMICs would benefit from a comprehensive approach that integrates services related to NCDs and communicable diseases such as HIV.[190] Beyond the above-described interventions for specifically ACS and IHD, overall cardiovascular care in LMICs would benefit from strengthening health systems, improving quality of care, optimizing human resources for health, establishing secure supply chains of drugs and technology, and promoting equitable access to care. Instead of vertical, disease-specific programs, a “diagonal” approach in which cardiovascular-related health care delivery is integrated into a comprehensive approach to health systems strengthening will likely yield superior results[191-195]. In order to maximize the effectiveness of health sector-specific interventions, they should be implemented in the context of broader population-level policy changes and community-level programs.

Thus, the remaining intervention necessary – perhaps underlying all of the above interventions – is comprehensive intersectoral policy dedicated to NCDs in general.[135,196,197] The roots of IHD risk are not contained solely within the health sector, and the entire spectrum of stakeholders are required to commit to policies and programs that will create the conditions that improve cardiovascular health. This would include, at a minimum, representation from the health, education, infrastructure, transportation, urban planning, trade, and finance sectors. In addition, productive partnerships among government, private sector, and civil society are possible and required.

Finally, although the large global burden of NCDs is well-established, funding from donors does not match this reality. In 2010, although NCDs collectively accounted for 49.8% of DALY burden of disease, they received only 2.3% of development assistance for health.[198] Within the WHO’s own budget, only 12% was allocated to NCDs for the 2006-2007 fiscal year, out of line with disease burden.[199] Analysis of spending by donors broadly, including private philanthropies such as the Gates Foundation, showed a similarly skewed allocation, with HIV/AIDS accounting for the largest portion of health spending, far in excess of its DALY-measured burden compared to NCDs and to other communicable diseases.[200] Another study reported spending of $0.78 per DALY for NCDs versus $23.90 per DALY for HIV, TB, and malaria.[201] While funding for NCDs has increased over the past decade,[198,201] allocation of funding that is more in-line with actual disease burden may aid the achievement of an array of global health goals,. The prospects for improving this balance of funding are challenging and require greater participation among aid recipient countries and alignment of UN institutions around NCD goals.[202] At the country level, health insurance and payment systems ideally should ensure equitable access to both in-hospital treatment of ACS as well as long-term outpatient access to medications and rehabilitative services.[203] In addition, public-private partnerships and other innovative financing mechanisms will be required.

Conclusion

Similar to the situation in HICs decades ago, LMICs today are well into a transition toward increasing morbidity and mortality from ACS and IHD. However, there are features that distinguish the patterns of ACS in LMICs from HICs. First, the death toll falls more heavily upon younger, productive ages in LMICs than in HICs, with mortality rates among adults aged 15-49 in some LMICs nearly double that in HICs. Second, the rate of the epidemiologic transition to increased burden from IHD has happened more rapidly in LMICs today than in HICs in the past. In addition, ACS and IHD are not diseases confined to the privileged classes; rather, there is a significant burden that also falls hard upon the lower-income strata in LMICs, who often are unable to afford the costs of medical therapy for primary or secondary prevention of IHD, let alone the expensive treatments for ACS that have helped make acute events more survivable in HICs. Together, these help explain the substantial economic burden that is anticipated from ACS and IHD if no action is taken.

Despite the immense burden, the global community is aided by new knowledge and discoveries made during the past half century. We continue to evolve more efficient and efficacious treatment strategies for ACS, ranging from rapid transport of patients to hospitals via emergency medical systems, to timely reperfusion, through to long-term cardiac rehabilitation, optimal medical therapy and risk factor control. We understand what the underlying risk factors for ACS are and how to prevent them through cardiovascular health promotion activities throughout the life course, appropriate therapeutic strategies, and intersectoral policy. The scientific challenge is primarily in translating this existing knowledge to new settings. In addition, the growing body of ACS literature from LMICs highlights the importance of local, national, and regional registries as important sources of information about current practices and inspiration for improvement and change.[115,204]

The critical task is implementation: the tools that we have need to be materialized. This involves engaging in health promotion activities in early childhood, ensuring access to essential medicines to treat and prevent ACS, developing resource- and context-specific clinical guidelines, implementing laws and regulations to protect the public's health from harmful products, planning the growth of cities to promote healthy behavior, and support from donor countries and international organizations to match the scale of the global burden of ACS, IHD, and other NCDs. We are well-equipped to confront this challenge so long as our will meets it.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

The authors would like to thank Claire Hutchinson for editorial assistance.

Funding: RV receives partial salary support from the Fogarty International Center of the National Institutes of Health under Award Number K01 TW 009218 - 03. BS is supported by the Stanford Interdisciplinary Graduate Fellowship and partly by NIA grant R24AG0393345. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

References

1. Lozano R, Naghavi M, Foreman K, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet. 2012; 380:2095–2128. [PubMed: 23245604]
2. Murray CJL, Vos T, Lozano R, et al. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet. 2012; 380:2197–2223. [PubMed: 23245608]
3. Bloom, DE.; Cafiero, ET.; Jané-Llopis, E.; Abrahams-Gessel, S.; Bloom, LR.; Fathima, S.; Feigl, AB.; Gaziano, T.; Mowafi, M.; Pandya, A.; Prettner, K.; Rosenberg, L.; Seligman, B.; Stein, AZ.; Weinstein, C., et al. The Global Economic Burden of Non-communicable Diseases. Geneva: 2011.
4. Danaei G, Finucane MM, Lin JK, Singh GM, Paciorek CJ, Cowan MJ, Farzadfar F, Stevens GA, Lim SS, Riley LM, Ezzati M. National, regional, and global trends in systolic blood pressure since 1980: systematic analysis of health examination surveys and epidemiological studies with 786 country-years and 5·4 million participants. Lancet. 2011; 377:568–77. [PubMed: 21295844]
5. Farzadfar F, Finucane MM, Danaei G, Pelizzari PM, Cowan MJ, Paciorek CJ, Singh GM, Lin JK, Stevens GA, Riley LM, Ezzati M. National, regional, and global trends in serum total cholesterol since 1980: systematic analysis of health examination surveys and epidemiological studies with 321 country-years and 3·0 million participants. Lancet. 2011; 377:578–86. [PubMed: 21295847]
6. Finucane MM, Stevens GA, Cowan MJ, Danaei G, Lin JK, Paciorek CJ, Singh GM, Gutierrez HR, Lu Y, Bahalim AN, Farzadfar F, Riley LM, Ezzati M. National, regional, and global trends in body-mass index since 1980: systematic analysis of health examination surveys and epidemiological studies with 960 country-years and 9·1 million participants. Lancet. 2011; 377:557–67. [PubMed: 21295846]
7. Rivera JA, Barquera S, González-Cossío T, Olaiz G, Sepúlveda J. Nutrition Transition in Mexico and in Other Latin American Countries. Nutr Rev. 2004; 62:S149–S157. [PubMed: 15387482]
8. Shetty PS. Nutrition transition in India. Public Health Nutr. 2002; 5:175–82. [PubMed: 12027282]
9. Omran AR. The epidemiologic transition. A theory of the epidemiology of population change. Milbank Mem Fund Q. 1971; 49:509–38. [PubMed: 5155251]
10. Yusuf S, Reddy S, Ounpuu S, Anand S. Global Burden of Cardiovascular Diseases: Part I: General Considerations, the Epidemiologic Transition, Risk Factors, and Impact of Urbanization. Circulation. 2001; 104:2746–2753. [PubMed: 11723030]
11. Olshansky SJ, Ault AB. The fourth stage of the epidemiologic transition: the age of delayed degenerative diseases. Milbank Q. 1986; 64:355–91. [PubMed: 3762504]
12. Gaziano JM. Fifth phase of the epidemiologic transition: the age of obesity and inactivity. JAMA. 2010; 303:275–6. [PubMed: 20071469]
13. Frenk J, Bobadilla JL, Sepúlveda J, Cervantes ML. Health transition in middle-income countries: new challenges for health care. Health Policy Plan. 1989; 4:29–39.
14. Boutayeb A. The double burden of communicable and non-communicable diseases in developing countries. Trans R Soc Trop Med Hyg. 2006; 100:191–9. [PubMed: 16274715]
15. Remais JV, Zeng G, Li G, Tian L, Engelgau MM. Convergence of non-communicable and infectious diseases in low- and middle-income countries. Int J Epidemiol. 2013; 42:221–7. [PubMed: 23064501]
16. Bygbjerg IC. Double burden of noncommunicable and infectious diseases in developing countries. Science. 2012; 337:1499–501. [PubMed: 22997329]
17. Gaziano, TA.; Reddy, KS.; Paccaud, F.; Horton, S.; Chaturvedi, V. Cardiovascular Disease. In: Jamison, DT.; Breman, JG.; Measham, AR., et al., editors. Disease Control Priorities in Developing Countries. 2. World Bank; 2006.
18. Moran AE, Forouzanfar MH, Roth G, Mensah GA, Ezzati M, Flaxman A, Murray CJL, Naghavi M. The Global Burden of Ischemic Heart Disease in 1990 and 2010: The Global Burden of Disease 2010 Study. Circulation. 2014; 129:1493–1501. [PubMed: 24573351]
19. Moran AE, Forouzanfar MH, Roth G, Mensah G, Ezzati M, Murray CJL, Naghavi M. Temporal Trends in Ischemic Heart Disease Mortality in 21 World Regions, 1980-2010: The Global Burden of Disease 2010 Study. Circulation. 2014; 129:1483–1492. [PubMed: 24573352]

20. Yach D, Hawkes C, Gould CL, Hofman KJ. The global burden of chronic diseases: overcoming impediments to prevention and control. JAMA. 2004; 291:2616–22. [PubMed: 15173153]
21. Ali MK, Rabadán-Diehl C, Flanigan J, Blanchard C, Narayan KMV, Engelgau M. Systems and capacity to address noncommunicable diseases in low- and middle-income countries. Sci Transl Med. 2013; 5:181cm4.
22. Ezzati, M.; Vander Hoorn, S.; Lawes, CMM.; Leach, R.; James, WPT.; Lopez, AD.; Rodgers, A.; Murray, CJL. Rethinking the “diseases of affluence” paradigm: global patterns of nutritional risks in relation to economic development. In: Novotny, T., editor. PLoS Med. Vol. 2. 2005. p. e133
23. Huffman, MD.; Rao, KD.; Pichon-Riviere, A., et al. A cross-sectional study of the microeconomic impact of cardiovascular disease hospitalization in four low- and middle-income countries. In: Malaga, G., editor. PLoS One. Vol. 6. 2011. p. e20821
24. Binnendijk E, Koren R, Dror DM. Can the rural poor in India afford to treat non-communicable diseases. Trop Med Int Heal. 2012; 17:1376–85.
25. Wang Y, Monteiro C, Popkin BM. Trends of obesity and underweight in older children and adolescents in the United States, Brazil, China, and Russia. Am J Clin Nutr. 2002; 75:971–977. [PubMed: 12036801]
26. Wang H, Du S, Zhai F, Popkin BM. Trends in the distribution of body mass index among Chinese adults, aged 20-45 years (1989-2000). Int J Obes (Lond). 2007; 31:272–8. [PubMed: 16788569]
27. Stevens GA, Singh GM, Lu Y, Danaei G, Lin JK, Finucane MM, Bahalim AN, McIntire RK, Gutierrez HR, Cowan M, Paciorek CJ, Farzadfar F, Riley L, Ezzati M. National, regional, and global trends in adult overweight and obesity prevalences. Popul Health Metr. 2012; 10:22. [PubMed: 23167948]
28. Ng M, Freeman MK, Fleming TD, Robinson M, Dwyer-Lindgren L, Thomson B, Wollum A, Sanman E, Wulf S, Lopez AD, Murray CJL, Gakidou E. Smoking prevalence and cigarette consumption in 187 countries, 1980-2012. JAMA. 2014; 311:183–92. [PubMed: 24399557]
29. Giovino GA, Mirza SA, Samet JM, Gupta PC, Jarvis MJ, Bhala N, Peto R, Zatonski W, Hsia J, Morton J, Palipudi KM, Asma S. Tobacco use in 3 billion individuals from 16 countries: an analysis of nationally representative cross-sectional household surveys. Lancet. 2012; 380:668–79. [PubMed: 22901888]
30. Monteiro CA, Cavalcante TM, Moura EC, Claro RM, Szwarcwald CL. Population-based evidence of a strong decline in the prevalence of smokers in Brazil (1989-2003). Bull World Health Organ. 2004; 85:527–534. [PubMed: 17768501]
31. Peer N, Bradshaw D, Laubscher R, Steyn K. Trends in adult tobacco use from two South African demographic and health surveys conducted in 1998 and 2003. SAMJ South African Med J. 2009; 99:744–749.
32. Jha P, Peto R. Global Effects of Smoking, of Quitting, and of Taxing Tobacco. N Engl J Med. 2014; 370:60–68. [PubMed: 24382066]
33. Stuckler D, McKee M, Ebrahim S, Basu S. Manufacturing epidemics: the role of global producers in increased consumption of unhealthy commodities including processed foods, alcohol, and tobacco. PLoS Med. 2012; 9:e1001235. [PubMed: 22745605]
34. Hallal PC, Andersen LB, Bull FC, Guthold R, Haskell W, Ekelund U. Global physical activity levels: surveillance progress, pitfalls, and prospects. Lancet. 2012; 380:247–57. [PubMed: 22818937]
35. Lim SS, Vos T, Flaxman AD, et al. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet. 2012; 380:2224–2260. [PubMed: 23245609]
36. Puffer RR, Verhoestraete LJ. Mortality from cardiovascular diseases in various countries, with special reference to atherosclerotic heart disease: a preliminary analysis. Bull World Health Organ. 1958; 19:315–24. [PubMed: 13585078]
37. Campbell M. The Main Cause of Increased Death Rate From Disease of the Heart: 1920 to 1959. BMJ. 1963; 2:712–7. [PubMed: 14043730]
38. Hechter HH, Borhani NO. Mortality and Geographic Distribution of Arteriosclerotic Heart Disease. Public Health Rep. 1965; 80:11–24. [PubMed: 14255446]

39. Levi F. Trends in mortality from cardiovascular and cerebrovascular diseases in Europe and other areas of the world. Heart. 2002; 88:119–124. [PubMed: 12117828]
40. Rosamond WD, Chambless LE, Heiss G, Mosley TH, Coresh J, Whitsel E, Wagenknecht L, Ni H, Folsom AR. Twenty-two-year trends in incidence of myocardial infarction, coronary heart disease mortality, and case fatality in 4 US communities, 1987-2008. Circulation. 2012; 125:1848–57. [PubMed: 22420957]
41. Nabel EG, Braunwald E. A Tale of Coronary Artery Disease and Myocardial Infarction. N Engl J Med. 2012; 366:54–63. [PubMed: 22216842]
42. Ford ES, Capewell S. Proportion of the Decline in Cardiovascular Mortality Disease due to Prevention Versus Treatment: Public Health Versus Clinical Care. Annu Rev Public Health. 2011; 32:5–22. [PubMed: 21417752]
43. Tunstall-Pedoe H, Vanuzzo D, Hobbs M, Mähönen M, Cepaitis Z, Kuulasmaa K, Keil U. Estimation of contribution of changes in coronary care to improving survival, event rates, and coronary heart disease mortality across the WHO MONICA Project populations. Lancet. 2000; 355:688–700. [PubMed: 10703800]
44. Kuulasmaa K, Tunstall-Pedoe H, Dobson A, Fortmann S, Sans S, Tolonen H, Evans A, Ferrario M. Estimation of contribution of changes in classic risk factors to trends in coronary-event rates across the WHO MONICA Project populations. Lancet. 2000; 355:675–687. [PubMed: 10703799]
45. Julian D. The evolution of the coronary care unit. Cardiovasc Res. 2001; 51:621–624. [PubMed: 11530092]
46. Gruppo Italiano per lo Studio della Streptochinasi nell'Infarto Miocardico (GISSI). Effectiveness of Intravenous Thrombolytic Treatment in Acute Myocardial Infarction. Lancet. 1986; 327:397–402.
47. The International Study Group. In-hospital mortality and clinical course of 20 891 patients with suspected acute myocardial infarction randomised between alteplase and streptokinase with or without heparin. Lancet. 1990; 336:71–75. [PubMed: 1975322]
48. Grüntzig AR, Senning Å, Siegenthaler WE. Nonoperative Dilatation of Coronary-Artery Stenosis. N Engl J Med. 1979; 301:61–68. [PubMed: 449946]
49. Malach M, Imperato PJ. Acute Myocardial Infarction and Acute Coronary Syndrome: Then and Now (1950-2005). Prev Cardiol. 2006; 9:228–234. [PubMed: 17085986]
50. So DYF, Ha ACT, Turek MA, Maloney JP, Higginson LA, Davies RF, Ryan SC, Le May MR. Comparison of mortality patterns in patients with ST-elevation myocardial infarction arriving by emergency medical services versus self-transport (from the prospective Ottawa Hospital STEMI Registry). Am J Cardiol. 2006; 97:458–61. [PubMed: 16461036]
51. Mathews R, Peterson ED, Li S, Roe MT, Glickman SW, Wiviott SD, Saucedo JF, Antman EM, Jacobs AK, Wang TY. Use of emergency medical service transport among patients with ST-segment-elevation myocardial infarction: findings from the National Cardiovascular Data Registry Acute Coronary Treatment Intervention Outcomes Network Registry-Get With The Guidelines. Circulation. 2011; 124:154–63. [PubMed: 21690494]
52. Tan L-L, Wong H-B, Poh C-L, Chan MY, Seow S-C, Yeo T-C, Teo S-G, Ooi SBS, Tan H-C, Lee C-H. Utilisation of emergency medical service among Singapore patients presenting with ST-segment elevation myocardial infarction: prevalence and impact on ischaemic time. Intern Med J. 2011; 41:809–14. [PubMed: 20546061]
53. First International Study of Infarct Survival Collaborative Group. Randomised trial of intravenous atenolol among 16 027 cases of suspected acute myocardial infarction: ISIS-1. Lancet. 1986; 2:57–66. [PubMed: 2873379]
54. Baigent C, Collins R, Appleby P, Parish S, Sleight P, Peto R. ISIS-2: 10 year survival among patients with suspected acute myocardial infarction in randomised comparison of intravenous streptokinase, oral aspirin, both, or neither. The ISIS-2 (Second International Study of Infarct Survival) Collaborative Group. BMJ. 1998; 316:1337–43. [PubMed: 9563981]
55. ISIS-4 Collaborative Group. ISIS-4: a randomised factorial trial assessing early oral captopril, oral mononitrate, and intravenous magnesium sulphate in 58,050 patients with suspected acute myocardial infarction. ISIS-4 (Fourth International Study of Infarct Survival) Collaborative. Lancet. 1995; 345:669–85. [PubMed: 7661937]

56. Antiplatelet Trialists' Collaboration. Collaborative overview of randomised trials of antiplatelet therapy Prevention of death, myocardial infarction, and stroke by prolonged antiplatelet therapy in various categories of patients. BMJ. 1994; 308:81–106. [PubMed: 8298418]
57. Freemantle N, Cleland J, Young P, Mason J, Harrison J. Beta Blockade after myocardial infarction: systematic review and meta regression analysis. BMJ. 1999; 318:1730–1737. [PubMed: 10381708]
58. Antithrombotic Trialists' Collaboration. Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. BMJ. 2002; 324:71–86. [PubMed: 11786451]
59. ACE Inhibitor Myocardial Infarction Collaborative Group. Indications for ACE Inhibitors in the Early Treatment of Acute Myocardial Infarction : Systematic Overview of Individual Data From 100 000 Patients in Randomized Trials. Circulation. 1998; 97:2202–2212. [PubMed: 9631869]
60. Scandinavian Simvastatin Survival Study Group. Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S). Lancet. 1994; 344:1383–9. [PubMed: 7968073]
61. Sacks FM, Pfeffer MA, Moye LA, Rouleau JL, Rutherford JD, Cole TG, Brown L, Warnica JW, Arnold JMO, Wun C-C, Davis BR, Braunwald E. The Effect of Pravastatin on Coronary Events after Myocardial Infarction in Patients with Average Cholesterol Levels. N Engl J Med. 1996; 335:1001–1009. [PubMed: 8801446]
62. Schwartz GG. Effects of Atorvastatin on Early Recurrent Ischemic Events in Acute Coronary Syndromes. JAMA. 2001; 285:1711. [PubMed: 11277825]
63. Cannon CP, Braunwald E, McCabe CH, Rader DJ, Rouleau JL, Belder R, Joyal SV, Hill KA, Pfeffer MA, Skene AM. Intensive versus Moderate Lipid Lowering with Statins after Acute Coronary Syndromes. N Engl J Med. 2004; 350:1495–1504. [PubMed: 15007110]
64. Pedersen TR, Faergeman O, Kastelein JJP, Olsson AG, Tikkanen MJ, Holme I, Larsen ML, Bendiksen FS, Lindahl C, Szarek M, Tsai J. High-dose atorvastatin vs usual-dose simvastatin for secondary prevention after myocardial infarction: the IDEAL study: a randomized controlled trial. JAMA. 2005; 294:2437–45. [PubMed: 16287954]
65. Kannel WB, Schwartz MJ, McNamara PM. Blood pressure and risk of coronary heart disease: the Framingham study. Dis Chest. 1969; 56:43–52. [PubMed: 5789839]
66. Kannel WB, Castelli WP, Gordon T, McNamara PM. Serum Cholesterol, Lipoproteins, and the Risk of Coronary Heart DiseaseThe Framingham Study. Ann Intern Med. 1971; 74:1–12. [PubMed: 5539274]
67. Farchi G, Capocaccia R, Verdecchia A, Menotti A, Keys A. Risk Factors Changes and Coronary Heart Disease in an Observational Study. Int J Epidemiol. 1981; 10:31–40. [PubMed: 7239760]
68. Kromhout D. Prevention of Coronary Heart Disease by Diet and Lifestyle: Evidence From Prospective Cross-Cultural, Cohort, and Intervention Studies. Circulation. 2002; 105:893–898. [PubMed: 11854133]
69. Kotchen TA. Historical trends and milestones in hypertension research: a model of the process of translational research. Hypertension. 2011; 58:522–38. [PubMed: 21859967]
70. Moser M. Historical Perspectives on the Management of Hypertension. J Clin Hypertens. 2006; 8:15–20.
71. Veterans Administration Cooperative Study Group on Anti-hypertensive Agents. Effects of Treatment on Morbidity in Hypertension: Results in Patients With Diastolic Blood Pressures Averaging 115 Through 129 mm Hg. JAMA J Am Med Assoc. 1967; 202:1028.
72. Lipid Research Clinics Program. The Lipid Research Clinics Coronary Primary Prevention Trial Results. JAMA. 1984; 251:351. [PubMed: 6361299]
73. Hjermann I, Holme I, Byre KV, Leren P. Effect of Diet and Smoking Iinterention On the Incidence of Coronary Heart Disease. Lancet. 1981; 318:1303–1310. [PubMed: 6118715]
74. Puska P, Nissinen A, Tuomilehto J, Salonen JT, Koskela K, McAlister A, Kottke TE, Maccoby N, Farquhar JW. The community-based strategy to prevent coronary heart disease: conclusions from the ten years of the North Karelia project. Annu Rev Public Health. 1985; 6:147–93. [PubMed: 3873246]

75. Farquhar JW. Effects of Communitywide Education on Cardiovascular Disease Risk Factors. JAMA. 1990; 264:359. [PubMed: 2362332]
76. James PA, Oparil S, Carter BL, et al. 2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults: Report From the Panel Members Appointed to the Eighth Joint National Committee (JNC 8). JAMA. 2013; 311:507–520. [PubMed: 24352797]
77. Eckel RH, Jakicic JM, Ard JD, et al. 2013 AHA/ACC Guideline on Lifestyle Management to Reduce Cardiovascular Risk: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation. 2013
78. Stone NJ, Robinson J, Lichtenstein AH, et al. 2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation. 2013
79. National Institute for Health and Care Excellence. CG67 Lipid Modification. 2010
80. National Institute for Health and Care Excellence. CG127 Hypertension. 2011
81. McGreevy, P. State bans trans fats. The Los Angeles Times. http://articles.latimes.com/2008/jul/26/local/me-transfat26. Published July 26, 2008
82. FOOD PREPARATION AND FOOD ESTABLISHMENTS Section 81.08 Foods containing artificial trans fat. New York City:
83. Conference of the Parties to the WHO FCTC. WHO Framework Convention on Tobacco Control. 2003
84. Evans A, Tolonen H, Hense H-W, Ferrario M, Sans S, Kuulasmaa K. Trends in coronary risk factors in the WHO MONICA Project. Int J Epidemiol. 2001; 30:S35–S40. [PubMed: 11759849]
85. Gregg EW, Cheng YJ, Cadwell BL, Imperatore G, Williams DE, Flegal KM, Narayan KMV, Williamson DF. Secular trends in cardiovascular disease risk factors according to body mass index in US adults. JAMA. 2005; 293:1868–74. [PubMed: 15840861]
86. Egan BM, Zhao Y, Axon RN. US trends in prevalence, awareness, treatment, and control of hypertension, 1988-2008. JAMA. 2010; 303:2043–50. [PubMed: 20501926]
87. Cohen JD, Cziraky MJ, Cai Q, Wallace A, Wasser T, Crouse JR, Jacobson TA. 30-year trends in serum lipids among United States adults: results from the National Health and Nutrition Examination Surveys II, III, and 1999-2006. Am J Cardiol. 2010; 106:969–75. [PubMed: 20854959]
88. Garrett BE, Dube SR, Trosclair A, Caraballo RS, Pechacek TF. Cigarette Smoking — United States, 1965–2008. MMWR. 2011; 60:109–113. [PubMed: 21430635]
89. Flegal KM, Carroll MD, Kit BK, Ogden CL. Prevalence of obesity and trends in the distribution of body mass index among US adults, 1999-2010. JAMA. 2012; 307:491–7. [PubMed: 22253363]
90. King DE, Mainous AG, Carnemolla M, Everett CJ. Adherence to healthy lifestyle habits in US adults, 1988-2006. Am J Med. 2009; 122:528–34. [PubMed: 19486715]
91. Ford ES, Dietz WH. Trends in energy intake among adults in the United States: findings from NHANES. Am J Clin Nutr. 2013; 97:848–53. [PubMed: 23426032]
92. Shay CM, Ning H, Allen NB, Carnethon MR, Chiuve SE, Greenlund KJ, Daviglus ML, Lloyd-Jones DM. Status of cardiovascular health in US adults: prevalence estimates from the National Health and Nutrition Examination Surveys (NHANES) 2003-2008. Circulation. 2012; 125:45–56. [PubMed: 22095826]
93. Huffman MD, Capewell S, Ning H, Shay CM, Ford ES, Lloyd-Jones DM. Cardiovascular health behavior and health factor changes (1988-2008) and projections to 2020: results from the National Health and Nutrition Examination Surveys. Circulation. 2012; 125:2595–602. [PubMed: 22547667]
94. Leeder, S.; Raymond, S.; Greenberg, H.; Liu, H.; Esson, K. A Race Against Time: The Challenge of Cardiovascular Disease in Developing Economies. New York: 2004.
95. Prabhakaran D, Yusuf S, Mehta S, et al. Two-year outcomes in patients admitted with non-ST elevation acute coronary syndrome: results of the OASIS registry 1 and 2. Indian Heart J. 2005; 57:217–25. [PubMed: 16196178]
96. Srivastava A, Mohanty SK. Age and sex pattern of cardiovascular mortality, hospitalisation and associated cost in India. PLoS One. 2013; 8:e62134. [PubMed: 23667455]

97. Joshi P, Islam S, Pais P, Reddy S, Dorairaj P, Kazmi K, Pandey MR, Haque S, Mendis S, Rangarajan S, Yusuf S. Risk factors for early myocardial infarction in South Asians compared with individuals in other countries. JAMA. 2007; 297:286–94. [PubMed: 17227980]
98. Mohanan PP, Mathew R, Harikrishnan S, Krishnan MN, Zachariah G, Joseph J, Eapen K, Abraham M, Menon J, Thomas M, Jacob S, Huffman MD, Prabhakaran D. Presentation, management, and outcomes of 25 748 acute coronary syndrome admissions in Kerala, India: results from the Kerala ACS Registry. Eur Heart J. 2013; 34:121–9. [PubMed: 22961945]
99. Juárez-Herrera Ú, Jerjes-Sánchez C. Risk factors, therapeutic approaches, and in-hospital outcomes in Mexicans with ST-elevation acute myocardial infarction: the RENASICA II multicenter registry. Clin Cardiol. 2013; 36:241–8. [PubMed: 23494467]
100. Piegas LS, Avezum A, Guimarães HP, Muniz AJ, Reis HJL, dos Santos ES, Knobel M, de Souza R. Acute coronary syndrome behavior: results of a Brazilian registry. Arq Bras Cardiol. 2013; 100:502–10. [PubMed: 23657268]
101. Shavadia J, Yonga G, Otieno H. A prospective review of acute coronary syndromes in an urban hospital in sub-Saharan Africa. Cardiovasc J Afr. 2012; 23:318–21. [PubMed: 22836154]
102. Demirkan B, Ege MR, Doğan P, İpek EG, Güray U, Güray Y. Factors influencing the use of ambulance among patients with acute coronary syndrome: results of two centers in Turkey. Anadolu Kardiyol Derg. 2013; 13:516–22. [PubMed: 23835296]
103. Gao R, Patel A, Gao W, Hu D, Huang D, Kong L, Qi W, Wu Y, Yang Y, Harris P, Algert C, Groenestein P, Turnbull F. Prospective observational study of acute coronary syndromes in China: practice patterns and outcomes. Heart. 2008; 94:554–60. [PubMed: 17932092]
104. Saidi O, Ben Mansour N, O'Flaherty M, Capewell S, Critchley JA, Ben Romdhane H. Analyzing recent coronary heart disease mortality trends in Tunisia between 1997 and 2009. PLoS One. 2013; 8:e63202. [PubMed: 23658808]
105. Joshi R, Chow CK, Raju PK, Raju R, Reddy KS, Macmahon S, Lopez AD, Neal B. Fatal and nonfatal cardiovascular disease and the use of therapies for secondary prevention in a rural region of India. Circulation. 2009; 119:1950–5. [PubMed: 19332466]
106. Mattos L, Alberto Pe, Berwanger O, dos Santos ES, Reis HJL, Romano ER, Petriz JLF, Sousa ACS, Neuenschwander FC, Guimarães JI, de Andrade JP. Desfechos clínicos aos 30 dias do registro brasileiro das síndromes coronárias agudas (ACCEPT). Arq Bras Cardiol. 2013; 100:6–13. [PubMed: 23370816]
107. Puymirat E, Battler A, Birkhead J, et al. Euro Heart Survey 2009 Snapshot: regional variations in presentation and management of patients with AMI in 47 countries. Eur Hear journal Acute Cardiovasc care. 2013; 2:359–70.
108. Song X-T, Chen Y-D, Pan W-Q, Lü S-Z. Gender based differences in patients with acute coronary syndrome: findings from Chinese Registry of Acute Coronary Events (CRACE). Chin Med J (Engl). 2007; 120:1063–7. [PubMed: 17637223]
109. Ahmed E, Alhabib KF, El-Menyar A, Asaad N, Sulaiman K, Hersi A, Almahmeed W, Alsheikh-Ali AA, Amin H, Al-Motarreb A, Al Saif S, Singh R, Al-Lawati J, Al Suwaidi J. Age and clinical outcomes in patients presenting with acute coronary syndromes. J Cardiovasc Dis Res. 2013; 4:134–9. [PubMed: 24027372]
110. Yusufali AM, AlMahmeed W, Tabatabai S, Rao K, Binbrek A. Acute coronary syndrome registry from four large centres in United Arab Emirates (UAE-ACS Registry). Heart Asia. 2010; 2:118–121.
111. Reddy KS. Cardiovascular diseases in the developing countries: dimensions, determinants, dynamics and directions for public health action. Public Health Nutr. 2006; 5:231–237. [PubMed: 12027289]
112. Critchley J, Liu J, Zhao D, Wei W, Capewell S. Explaining the increase in coronary heart disease mortality in Beijing between 1984 and 1999. Circulation. 2004; 110:1236–44. [PubMed: 15337690]
113. Srimahachota S, Kanjanavanit R, Boonyaratavej S, Boonsom W, Veerakul G, Tresukosol D. Demographic, management practices and in-hospital outcomes of Thai Acute Coronary Syndrome Registry (TACSR): the difference from the Western world. J Med Assoc Thai. 2007; 90(Suppl 1):1–11. [PubMed: 18431881]

114. Srimahachota S, Boonyaratavej S, Kanjanavanit R, Sritara P, Krittayaphong R, Kunjara-Naayudhya R, Tatsanavivat P. Thai Registry in Acute Coronary Syndrome (TRACS)--an extension of Thai Acute Coronary Syndrome registry (TACS) group: lower in-hospital but still high mortality at one-year. J Med Assoc Thail. 2012; 95:508–18.
115. Karthikeyan G, Xavier D, Prabhakaran D, Pais P. Perspectives on the management of coronary artery disease in India. Heart. 2007; 93:1334–8. [PubMed: 17933988]
116. ACCESS Investigators. Management of acute coronary syndromes in developing countries: Acute Coronary Events—a multinational Survey of current management Strategies. Am Heart J. 2011; 162:852–859.e22. [PubMed: 22093201]
117. Huffman MD, Prabhakaran D, Abraham AK, Krishnan MN, Nambiar AC, Mohanan PP. Optimal in-hospital and discharge medical therapy in acute coronary syndromes in Kerala: results from the Kerala acute coronary syndrome registry. Circ Cardiovasc Qual Outcomes. 2013; 6:436–43. [PubMed: 23800985]
118. Pagidipati, NJ.; Huffman, MD.; Jeemon, P., et al. Association between gender, process of care measures, and outcomes in ACS in India: results from the detection and management of coronary heart disease (DEMAT) registry. In: Schnabel, RB., editor. PLoS One. Vol. 8. 2013. p. e62061
119. Yusuf S, Islam S, Chow CK, et al. Use of secondary prevention drugs for cardiovascular disease in the community in high-income, middle-income, and low-income countries (the PURE Study): a prospective epidemiological survey. Lancet. 2011; 378:1231–43. [PubMed: 21872920]
120. Teo K, Lear S, Islam S, et al. Prevalence of a healthy lifestyle among individuals with cardiovascular disease in high-, middle- and low-income countries: The Prospective Urban Rural Epidemiology (PURE) study. JAMA. 2013; 309:1613–21. [PubMed: 23592106]
121. Mendis S, Abegunde D, Yusuf S, Ebrahim S, Shaper G, Ghannem H, Shengelia B. WHO study on Prevention of REcurrences of Myocardial Infarction and StrokE (WHO-PREMISE). Bull World Health Organ. 2005; 83:820–829. [PubMed: 16302038]
122. Orlandini A, Díaz R, Wojdyla D, Pieper K, Van de Werf F, Granger CB, Harrington RA, Boersma E, Califf RM, Armstrong P, White H, Simes J, Paolasso E. Outcomes of patients in clinical trials with ST-segment elevation myocardial infarction among countries with different gross national incomes. Eur Heart J. 2006; 27:527–33. [PubMed: 16410369]
123. Engelgau MM, Karan A, Mahal A. The Economic impact of Non-communicable Diseases on households in India. Global Health. 2012; 8:9. [PubMed: 22533895]
124. Kankeu HT, Saksena P, Xu K, Evans DB. The financial burden from non-communicable diseases in low- and middle-income countries: a literature review. Health Res Policy Syst. 2013; 11:31. [PubMed: 23947294]
125. Rahman, MM.; Gilmour, S.; Saito, E.; Sultana, P.; Shibuya, K. Health-related financial catastrophe, inequality and chronic illness in Bangladesh. In: van Baal, PHM., editor. PLoS One. Vol. 8. 2013. p. e56873
126. World Health Organization. Preventing Chronic Diseases: A Vital Investment. Geneva: World Health Organization; 2005.
127. Mayosi BM, Flisher AJ, Lalloo UG, Sitas F, Tollman SM, Bradshaw D. The burden of non-communicable diseases in South Africa. Lancet. 2009; 374:934–47. [PubMed: 19709736]
128. Basu S, Millett C. Social epidemiology of hypertension in middle-income countries: determinants of prevalence, diagnosis, treatment, and control in the WHO SAGE study. Hypertension. 2013; 62:18–26. [PubMed: 23670299]
129. Kinra S, Bowen LJ, Lyngdoh T, Prabhakaran D, Reddy KS, Ramakrishnan L, Gupta R, Bharathi AV, Vaz M, Kurpad AV, Smith GD, Ben-Shlomo Y, Ebrahim S. Sociodemographic patterning of non-communicable disease risk factors in rural India: a cross sectional study. BMJ. 2010; 341:c4974. [PubMed: 20876148]
130. Xavier D, Pais P, Devereaux PJ, et al. Treatment and outcomes of acute coronary syndromes in India (CREATE): a prospective analysis of registry data. Lancet. 2008; 371:1435–42. [PubMed: 18440425]
131. Pais P, Pogue J, Gerstein H, Zachariah E, Savitha D, Jayprakash S, Nayak P, Yusuf S. Risk factors for acute myocardial infarction in Indians: a case-control study. Lancet. 1996; 348:358–363. [PubMed: 8709733]

132. Fuster, V.; Bridget, B. Promoting Cardiovascular Health in the Developing World:A Critical Challenge to Achieve Global Health. The National Academies Press; 2010. Kelly EC on P the GE of CDM the C in DCI of M.
133. Fuster V, Kelly BB, Vedanthan R. Promoting global cardiovascular health: moving forward. Circulation. 2011; 123:1671–8. [PubMed: 21502585]
134. Kishore SP, Vedanthan R, Fuster V. Promoting global cardiovascular health ensuring access to essential cardiovascular medicines in low- and middle-income countries. J Am Coll Cardiol. 2011; 57:1980–7. [PubMed: 21565635]
135. Fuster V, Kelly BB, Vedanthan R. Global cardiovascular health: urgent need for an intersectoral approach. J Am Coll Cardiol. 2011; 58:1208–10. [PubMed: 21903051]
136. Gaziano TA, Pagidipati N. Scaling up chronic disease prevention interventions in lower- and middle-income countries. Annu Rev Public Health. 2013; 34:317–35. [PubMed: 23297660]
137. World Health Organization. Scaling up action against noncommunicable diseases: how much will it cost?. 2011
138. Biro FM, Wien M. Childhood obesity and adult morbidities. Am J Clin Nutr. 2010; 91:1499S–1505S. [PubMed: 20335542]
139. Agras WS, Hammer LD, McNicholas F, Kraemer HC. Risk factors for childhood overweight: a prospective study from birth to 9.5 years. J Pediatr. 2004; 145:20–5. [PubMed: 15238901]
140. Bjørge T, Engeland A, Tverdal A, Smith GD. Body mass index in adolescence in relation to cause-specific mortality: a follow-up of 230,000 Norwegian adolescents. Am J Epidemiol. 2008; 168:30–7. [PubMed: 18477652]
141. Freedman DS, Khan LK, Serdula MK, Dietz WH, Srinivasan SR, Berenson GS. The relation of childhood BMI to adult adiposity: the Bogalusa Heart Study. Pediatrics. 2005; 115:22–7. [PubMed: 15629977]
142. Bibbins-Domingo K, Coxson P, Pletcher MJ, Lightwood J, Goldman L. Adolescent overweight and future adult coronary heart disease. N Engl J Med. 2007; 357:2371–9. [PubMed: 18057339]
143. Cunningham SA, Kramer MR, Narayan KMV. Incidence of Childhood Obesity in the United States. N Engl J Med. 2014; 370:403–411. [PubMed: 24476431]
144. Céspedes J, Briceño G, Farkouh ME, Vedanthan R, Baxter J, Leal M, Boffetta P, Woodward M, Hunn M, Dennis R, Fuster V. Targeting preschool children to promote cardiovascular health: cluster randomized trial. Am J Med. 2013; 126:27–35.e3. [PubMed: 23062403]
145. Céspedes J, Briceño G, Farkouh ME, Vedanthan R, Baxter J, Leal M, Boffetta P, Hunn M, Dennis R, Fuster V. Promotion of cardiovascular health in preschool children: 36-month cohort follow-up. Am J Med. 2013; 126:1122–6. [PubMed: 24262725]
146. Draper CE, de Villiers A, Lambert EV, Fourie J, Hill J, Dalais L, Abrahams Z, Steyn NP. HealthKick: a nutrition and physical activity intervention for primary schools in low-income settings. BMC Public Health. 2010; 10:398. [PubMed: 20604914]
147. Foster GD, Linder B, Baranowski T, Cooper DM, Goldberg L, Harrell JS, Kaufman F, Marcus MD, Treviño RP, Hirst K. A school-based intervention for diabetes risk reduction. N Engl J Med. 2010; 363:443–53. [PubMed: 20581420]
148. Galvez MP, Hong L, Choi E, Liao L, Godbold J, Brenner B. Childhood obesity and neighborhood food-store availability in an inner-city community. Acad Pediatr. 2009; 9:339–43. [PubMed: 19560992]
149. Ritchie LD, Sharma S, Ikeda JP, Mitchell RA, Raman A, Green BS, Hudes ML, Fleming SE. Taking Action Together: a YMCA-based protocol to prevent type-2 diabetes in high-BMI inner-city African American children. Trials. 2010; 11:60. [PubMed: 20492667]
150. Birch LL, Ventura AK. Preventing childhood obesity: what works? Int J Obes. 2009; 33(Suppl 1):S74–81.
151. Progress in Preventing Childhood Obesity: How Do We Measure Up?. The National Academies Press; 2007. on Progress in Preventing Childhood Obesity C.
152. US Department of Health and Human Services. Strategic Plan for NIH obesity research: a report of the NIH Obesity Task Force. Bethesda: 2004.

153. Katz DL, O'Connell M, Njike VY, Yeh M-C, Nawaz H. Strategies for the prevention and control of obesity in the school setting: systematic review and meta-analysis. Int J Obes. 2008; 32:1780–9.

154. Peñalvo JL, Sotos-Prieto M, Santos-Beneit G, Pocock S, Redondo J, Fuster V. The Program SI! intervention for enhancing a healthy lifestyle in preschoolers: first results from a cluster randomized trial. BMC Public Health. 2013; 13:1208. [PubMed: 24359285]

155. Peñalvo JL, Santos-Beneit G, Sotos-Prieto M, Martínez R, Rodríguez C, Franco M, López-Romero P, Pocock S, Redondo J, Fuster V. A cluster randomized trial to evaluate the efficacy of a school-based behavioral intervention for health promotion among children aged 3 to 5. BMC Public Health. 2013; 13:656. [PubMed: 23855415]

156. Asaria P, Chisholm D, Mathers C, Ezzati M, Beaglehole R. Chronic disease prevention: health effects and financial costs of strategies to reduce salt intake and control tobacco use. Lancet. 2007; 370:2044–53. [PubMed: 18063027]

157. Willett, WC.; Koplan, JP.; Nugent, R.; Dusenbury, C.; Puska, P.; Gaziano, TA. Prevention of Chronic Disease by Means of Diet and Lifestyle Changes. In: Jamison, DT.; Breman, JG.; Measham, AR., et al., editors. Disease Control Priorities in Developing Countries. 2. World Bank; 2006.

158. Smit W, Hancock T, Kumaresen J, Santos-Burgoa C, Sánchez-Kobashi Meneses R, Friel S. Toward a research and action agenda on urban planning/design and health equity in cities in low and middle-income countries. J Urban Health. 2011; 88:875–85. [PubMed: 21858601]

159. Trowbridge MJ, Schmid TL. Built environment and physical activity promotion: place-based obesity prevention strategies. J Law Med Ethics. 2013; 41(Suppl 2):46–51. [PubMed: 24446998]

160. World Health Organization. Global recommendations on physical activity for health. 2010

161. Díaz Del Castillo A, Sarmiento OL, Reis RS, Brownson RC. Translating evidence to policy: urban interventions and physical activity promotion in Bogotá, Colombia and Curitiba, Brazil. Transl Behav Med. 2011; 1:350–60. [PubMed: 24073055]

162. Lachat, C.; Otchere, S.; Roberfroid, D.; Abdulai, A.; Seret, FMA.; Milesevic, J.; Xuereb, G.; Candeias, V.; Kolsteren, P. Diet and physical activity for the prevention of noncommunicable diseases in low- and middle-income countries: a systematic policy review. In: Cobiac, LJ., editor. PLoS Med. Vol. 10. 2013. p. e1001465

163. Jha, P.; Chaloupka, FJ., editors. Tobacco Control in Developing Countries. New York: Oxford University Press; 2000.

164. Jha, P.; Chaloupka, FJ.; Moore, J.; Gajalakshmi, V.; Gupta, PC.; Peck, R.; Asma, S.; Witold, Z. Tobacco Addiction. In: Jamison, DT.; Breman, JG.; Measham, AR., et al., editors. Disease Control Priorities in Developing Countries. 2. World Bank; 2006.

165. Piné-Abata H, McNeill A, Raw M, Bitton A, Rigotti N, Murray R. A survey of tobacco dependence treatment guidelines in 121 countries. Addiction. 2013; 108:1470–5. [PubMed: 23437892]

166. Mamudu HM, Hammond R, Glantz SA. Project Cerberus: tobacco industry strategy to create an alternative to the Framework Convention on Tobacco Control. Am J Public Health. 2008; 98:1630–42. [PubMed: 18633079]

167. Gonzalez M, Green LW, Glantz SA. Through tobacco industry eyes: civil society and the FCTC process from Philip Morris and British American Tobacco's perspectives. Tob Control. 2012; 21:e1. [PubMed: 21636611]

168. Bitton A, Green C, Colbert J. Improving the delivery of global tobacco control. Mt Sinai J Med. 2011; 78:382–93. [PubMed: 21598265]

169. Bitton A, Raw M, Richards A, McNeill A, Rigotti NA. A comparison of four international surveys of tobacco dependence treatment provision: implications for monitoring the Framework Convention on Tobacco Control. Addiction. 2010; 105:2184–91. [PubMed: 20735369]

170. Weishaar, H.; Collin, J.; Smith, K.; Grüning, T.; Mandal, S.; Gilmore, A. Global health governance and the commercial sector: a documentary analysis of tobacco company strategies to influence the WHO framework convention on tobacco control. In: Novotny, TE., editor. PLoS Med. Vol. 9. 2012. p. e1001249

171. Crosbie E, Sebrié EM, Glantz SA. Tobacco industry success in Costa Rica: the importance of FCTC article 5.3. Salud Publica Mex. 2012; 54:28–38. [PubMed: 22286826]

172. Nakkash R, Lee K. The tobacco industry's thwarting of marketing restrictions and health warnings in Lebanon. Tob Control. 2009; 18:310–6.

173. Lee S, Ling PM, Glantz SA. The vector of the tobacco epidemic: tobacco industry practices in low and middle-income countries. Cancer Causes Control. 2012; 23(Suppl 1):117–29. [PubMed: 22370696]

174. Lencucha R. Philip Morris versus Uruguay: health governance challenged. Lancet. 2010; 376:852–3. [PubMed: 20833287]

175. WHO Framework Convention on Tobacco Control Convention Secretariat. 2012 Global Progress Report on Implementation of the WHO Framework Convention on Tobacco Control. 2012

176. Smith KE, Gilmore AB, Fooks G, Collin J, Weishaar H. Tobacco industry attempts to undermine Article 5.3 and the "good governance" trap. Tob Control. 2009; 18:509–11. [PubMed: 19955541]

177. Berwanger O, Guimarães HP, Laranjeira LN, et al. Effect of a multifaceted intervention on use of evidence-based therapies in patients with acute coronary syndromes in Brazil: the BRIDGE-ACS randomized trial. JAMA. 2012; 307:2041–9. [PubMed: 22665103]

178. Gaziano TA, Opie LH, Weinstein MC. Cardiovascular disease prevention with a multidrug regimen in the developing world: a cost-effectiveness analysis. Lancet. 2006; 368:679–86. [PubMed: 16920473]

179. Lonn E, Bosch J, Teo KK, Pais P, Xavier D, Yusuf S. The polypill in the prevention of cardiovascular diseases: key concepts, current status, challenges, and future directions. Circulation. 2010; 122:2078–88. [PubMed: 21098469]

180. Sanz G, Fuster V. Prevention: Polypills for cardiovascular prevention: a step forward? Nat Rev Cardiol. 2013; 10:683–4. [PubMed: 24101102]

181. Sanz G, Fuster V, Guzmán L, Guglietta A, Arnáiz JA, Martínez F, Sarria A, Roncaglioni MC, Taubert K. The fixed-dose combination drug for secondary cardiovascular prevention project: improving equitable access and adherence to secondary cardiovascular prevention with a fixed-dose combination drug. Study design and objectives. Am Heart J. 2011; 162:811–817.e1. [PubMed: 22093195]

182. Sanz G, Fuster V. Fixed-dose combination therapy and secondary cardiovascular prevention: rationale, selection of drugs and target population. Nat Clin Pract Cardiovasc Med. 2009; 6:101–10. [PubMed: 19104519]

183. Elley, CR.; Gupta, AK.; Webster, R.; Selak, V.; Jun, M.; Patel, A.; Rodgers, A.; Thom, S. The efficacy and tolerability of "polypills": meta-analysis of randomised controlled trials. In: Wright, JM., editor. PLoS One. Vol. 7. 2012. p. e52145

184. Thom S, Poulter N, Field J, Patel A, Prabhakaran D, Stanton A, Grobbee DE, Bots ML, Reddy KS, Cidambi R, Bompoint S, Billot L, Rodgers A. Effects of a fixed-dose combination strategy on adherence and risk factors in patients with or at high risk of CVD: the UMPIRE randomized clinical trial. JAMA. 2013; 310:918–29. [PubMed: 24002278]

185. Bautista LE, Vera-Cala LM, Ferrante D, et al. A "polypill" aimed at preventing cardiovascular disease could prove highly cost-effective for use in Latin America. Health Aff. 2013; 32:155–64.

186. Huffman MD, Yusuf S. Polypills: Essential Medicines for Cardiovascular Disease Secondary Prevention? J Am Coll Cardiol. 2014

187. Cameron A, Ewen M, Ross-Degnan D, Ball D, Laing R. Medicine prices, availability, and affordability in 36 developing and middle-income countries: a secondary analysis. Lancet. 2009; 373:240–9. [PubMed: 19042012]

188. Mendis S, Fukino K, Cameron A, Laing R, Filipe A Jr, Khatib O, Leowski J, Ewen M. The availability and affordability of selected essential medicines for chronic diseases in six low- and middle-income countries. Bull World Health Organ. 2007; 85:279–288. [PubMed: 17546309]

189. Vedanthan R, Fuster V. Urgent need for human resources to promote global cardiovascular health. Nat Rev Cardiol. 2011; 8:114–7. [PubMed: 21045785]

190. Van Olmen J, Schellevis F, Van Damme W, Kegels G, Rasschaert F. Management of Chronic Diseases in Sub-Saharan Africa: Cross-Fertilisation between HIV/AIDS and Diabetes Care. J Trop Med. 2012; 2012 349312.

191. Frenk J. The global health system: strengthening national health systems as the next step for global progress. PLoS Med. 2010; 7:e1000089. [PubMed: 20069038]
192. Ooms G, Van Damme W, Baker BK, Zeitz P, Schrecker T. The “diagonal” approach to Global Fund financing: a cure for the broader malaise of health systems? Global Health. 2008; 4:6. [PubMed: 18364048]
193. Samb B, Evans T, Dybul M, Atun R, Moatti J-P, Nishtar S, Wright A, Celletti F, Hsu J, Kim JY, Brugha R, Russell A, Etienne C. An assessment of interactions between global health initiatives and country health systems. Lancet. 2009; 373:2137–69. [PubMed: 19541040]
194. Drobac PC, Basinga P, Condo J, et al. Comprehensive and integrated district health systems strengthening: the Rwanda Population Health Implementation and Training (PHIT) Partnership. BMC Health Serv Res. 2013; 13(Suppl 2):S5. [PubMed: 23819573]
195. Vasan A, Ellner A, Lawn SD, Gove S, Anatole M, Gupta N, Drobac P, Nicholson T, Seung K, Mabey DC, Farmer PE. Integrated care as a means to improve primary care delivery for adults and adolescents in the developing world: a critical analysis of Integrated Management of Adolescent and Adult Illness (IMAI). BMC Med. 2014; 12:6. [PubMed: 24423387]
196. Mendis S, Fuster V. National policies and strategies for noncommunicable diseases. Nat Rev Cardiol. 2009; 6:723–7. [PubMed: 19851350]
197. Narayan KMV, Ali MK, Koplan JP. Global Noncommunicable Diseases — Where Worlds Meet. N Engl J Med. 2010; 363:1196–1198. [PubMed: 20860499]
198. Dieleman JL, Graves CM, Templin T, Johnson E, Baral R, Leach-Kemon K, Haakenstad AM, Murray CJL. Global Health Development Assistance Remained Steady In 2013 But Did Not Align With Recipients’ Disease Burden. Health Aff (Millwood). 2014 hlthaff.2013.1432.
199. Stuckler D, King L, Robinson H, McKee M. WHO’s budgetary allocations and burden of disease: a comparative analysis. Lancet. 2008; 372:1563–9. [PubMed: 18984189]
200. Sridhar D, Batniji R. Misfinancing global health: a case for transparency in disbursements and decision making. Lancet. 2008; 372:1185–91. [PubMed: 18926279]
201. Nugent R, Feigl AB. Where Have All the Donors Gone? Scarce Donor Funding for Non-Communicable Diseases. 2010
202. Sridhar D, Brolan CE, Durrani S, Edge J, Gostin LO, Hill P, McKee M. Recent shifts in global governance: implications for the response to non-communicable diseases. PLoS Med. 2013; 10:e1001487. [PubMed: 23935458]
203. Vamadevan AS, Shah BR, Califf RM, Prabhakaran D. Cardiovascular research in India: a perspective. Am Heart J. 2011; 161:431–8. [PubMed: 21392596]
204. Gurm HS, Eagle KA. Channelling regional registries for optimization of cardiac care: lessons from around the world. Eur Heart J. 2013; 34:83–5. [PubMed: 23070025]
205. Armstrong GL, Conn LA, Pinner RW. Trends in infectious disease mortality in the United States during the 20th century. JAMA. 1999; 281:61–6. [PubMed: 9892452]
206. Institute for Health Metrics and Evaluation. GBD Compare. 2013
207. Unal B, Critchley JA, Capewell S. Explaining the decline in coronary heart disease mortality in England and Wales between 1981 and 2000. Circulation. 2004; 109:1101–7. [PubMed: 14993137]
208. Laatikainen T, Critchley J, Vartiainen E, Salomaa V, Ketonen M, Capewell S. Explaining the decline in coronary heart disease mortality in Finland between 1982 and 1997. Am J Epidemiol. 2005; 162:764–73. [PubMed: 16150890]
209. Bennett K, Kabir Z, Unal B, Shelley E, Critchley J, Perry I, Feely J, Capewell S. Explaining the recent decrease in coronary heart disease mortality rates in Ireland, 1985-2000. J Epidemiol Community Health. 2006; 60:322–7. [PubMed: 16537349]
210. Palmieri L, Bennett K, Giampaoli S, Capewell S. Explaining the decrease in coronary heart disease mortality in Italy between 1980 and 2000. Am J Public Health. 2010; 100:684–92. [PubMed: 19608958]
211. Capewell S, Beaglehole R, Seddon M, McMurray J. Explanation for the Decline in Coronary Heart Disease Mortality Rates in Auckland, New Zealand, Between 1982 and 1993. Circulation. 2000; 102:1511–1516. [PubMed: 11004141]

212. Capewell S, Morrison CE, McMurray JJ. Contribution of modern cardiovascular treatment and risk factor changes to the decline in coronary heart disease mortality in Scotland between 1975 and 1994. Heart. 1999; 81:380–386. [PubMed: 10092564]

213. Björck L, Rosengren A, Bennett K, Lappas G, Capewell S. Modelling the decreasing coronary heart disease mortality in Sweden between 1986 and 2002. Eur Heart J. 2009; 30:1046–56. [PubMed: 19141562]

214. Ford ES, Ajani UA, Croft JB, Critchley JA, Labarthe DR, Kottke TE, Giles WH, Capewell S. Explaining the Decrease in U.S. Deaths from Coronary Disease, 1980–2000. N Engl J Med. 2007; 356:2388–2398. [PubMed: 17554120]

Abbreviations and Acronyms

ACE	angiotensin-converting enzyme
ACS	acute coronary syndrome
DALY	disability-adjusted life year
HICs	high-income countries
IHD	ischemic heart disease
LMICs	low- and middle-income countries
NCDs	non-communicable diseases
WHO	World Health Organization

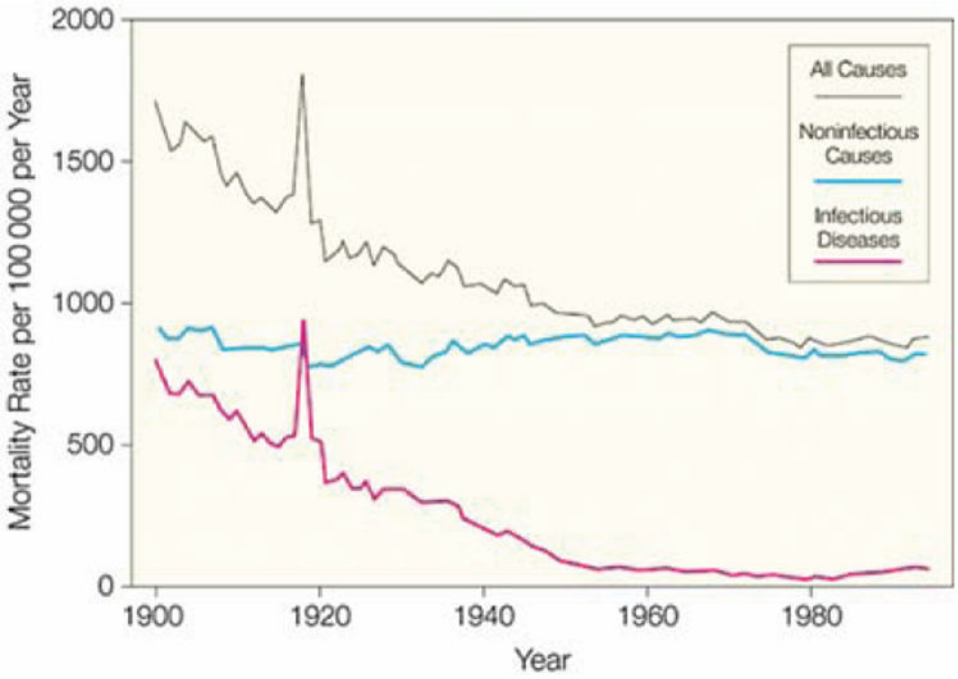

Figure 1.

The epidemiologic transition in the United States, which was already well underway by 1900. From: JAMA. 1999;281(1):61-66.[205]

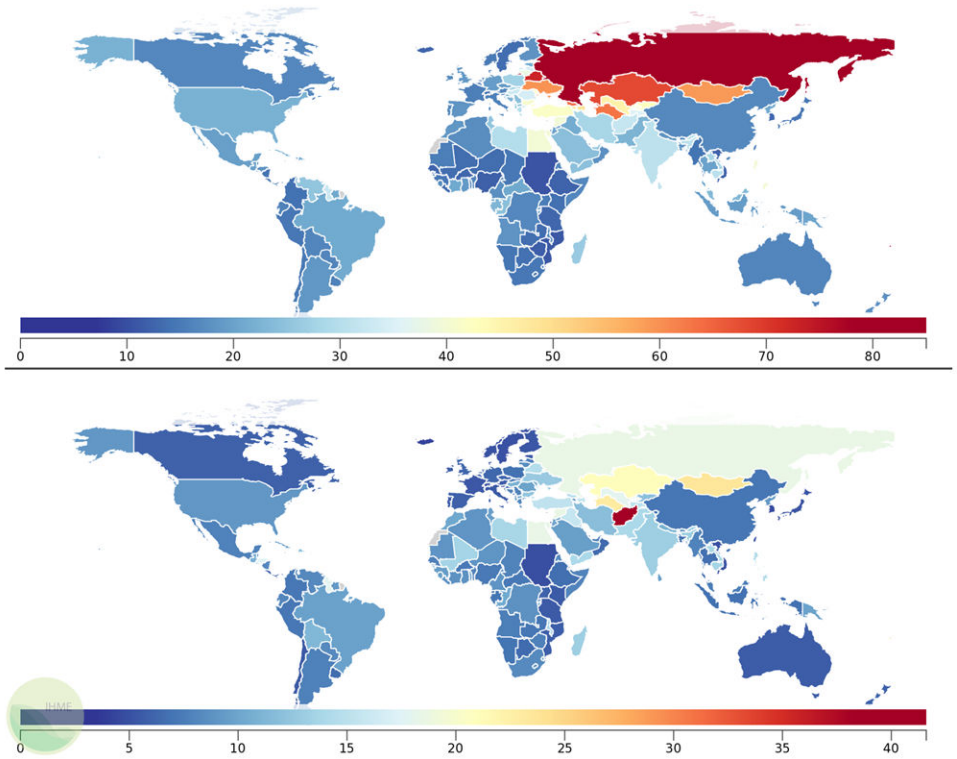

Figure 2.

Mortality rates from IHD per 100,000 in 2010 by country, ages 15-49, males (top) and females (bottom). Data from 2012 Global Burden of Disease.[206]

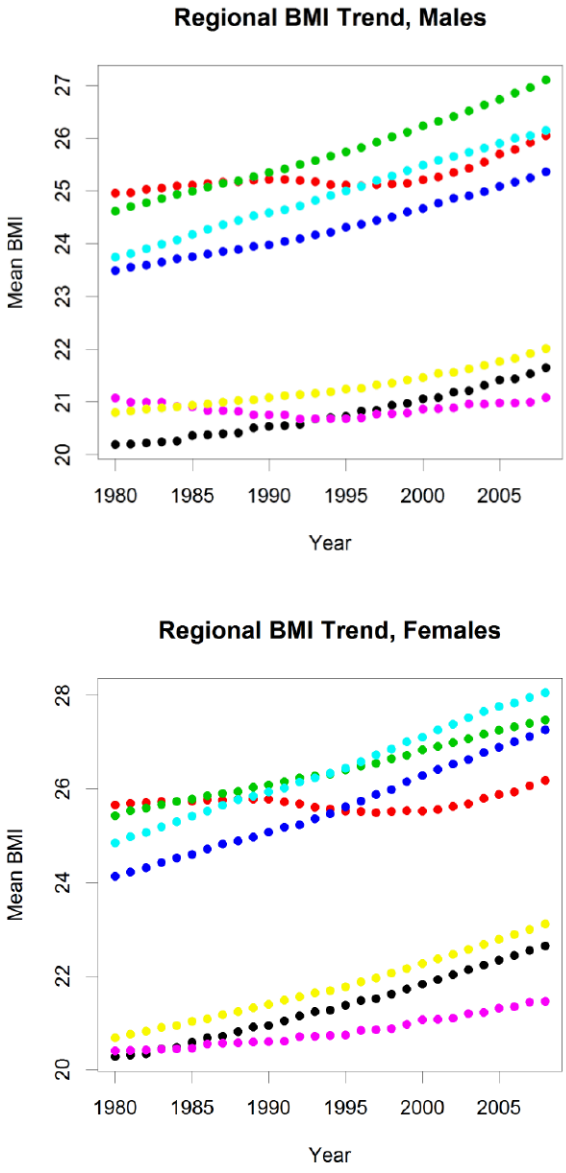

Figure 3.

Age-standardized mean body-mass index (BMI) by sex and region. Green: high-income countries, Black: East Asia/Pacific, Red: Eastern Europe/Central Asia, Dark Blue: Latin America/Caribbean, Light Blue: Middle East/North Africa, Purple: South Asia, Yellow: Sub-Saharan Africa.

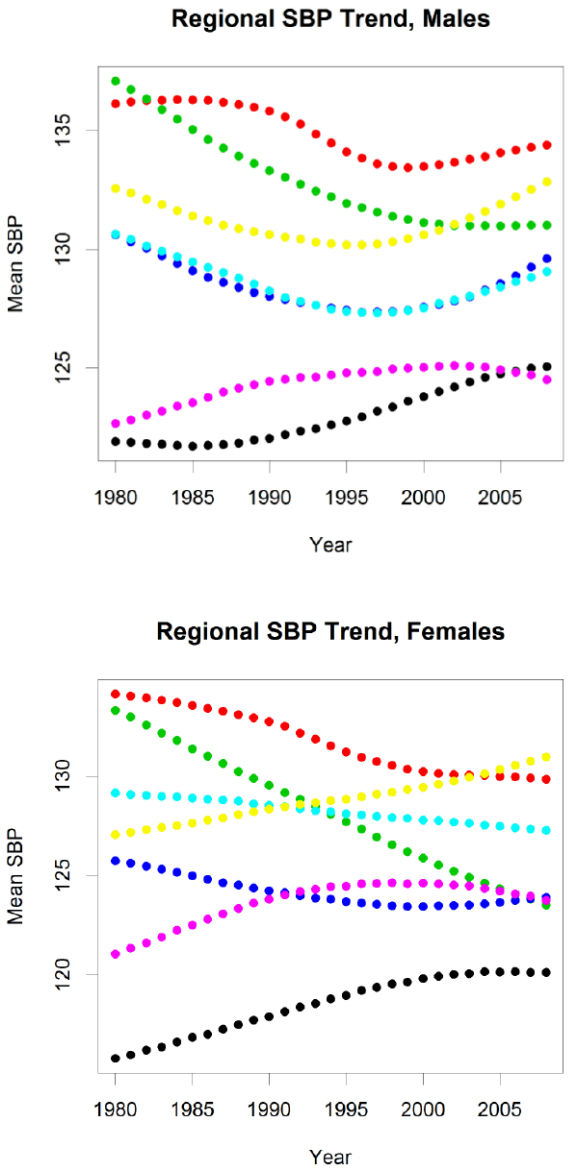

Figure 4.

Age-standardized mean systolic blood pressure (SBP) by sex and region. Color coding as in Figure 3.

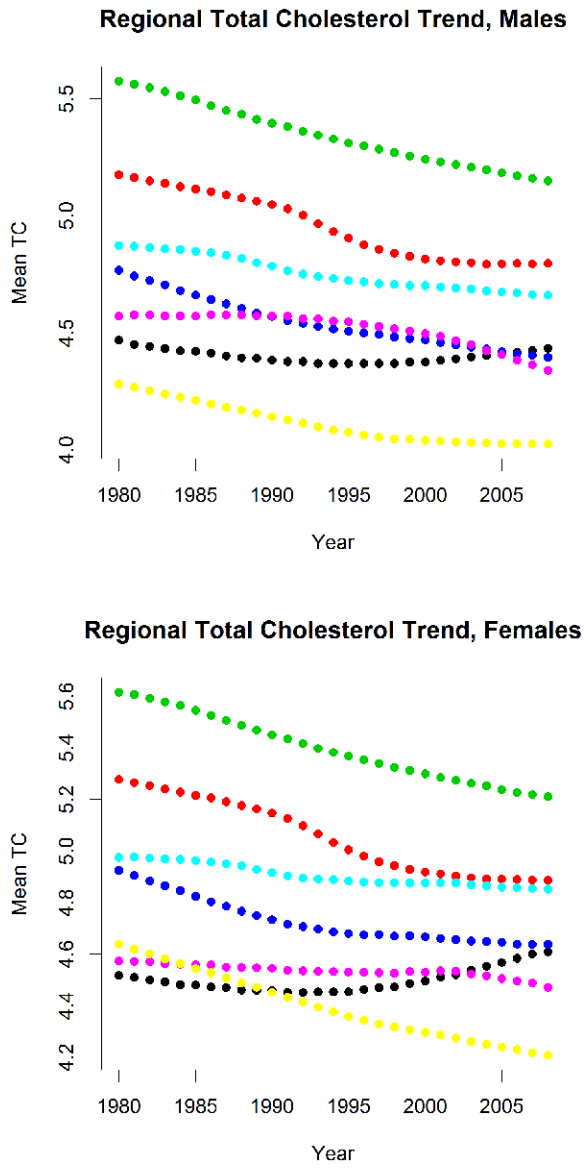

Figure 5.
Age-standardized mean total cholesterol by sex and region. Color coding as in Figure 3.

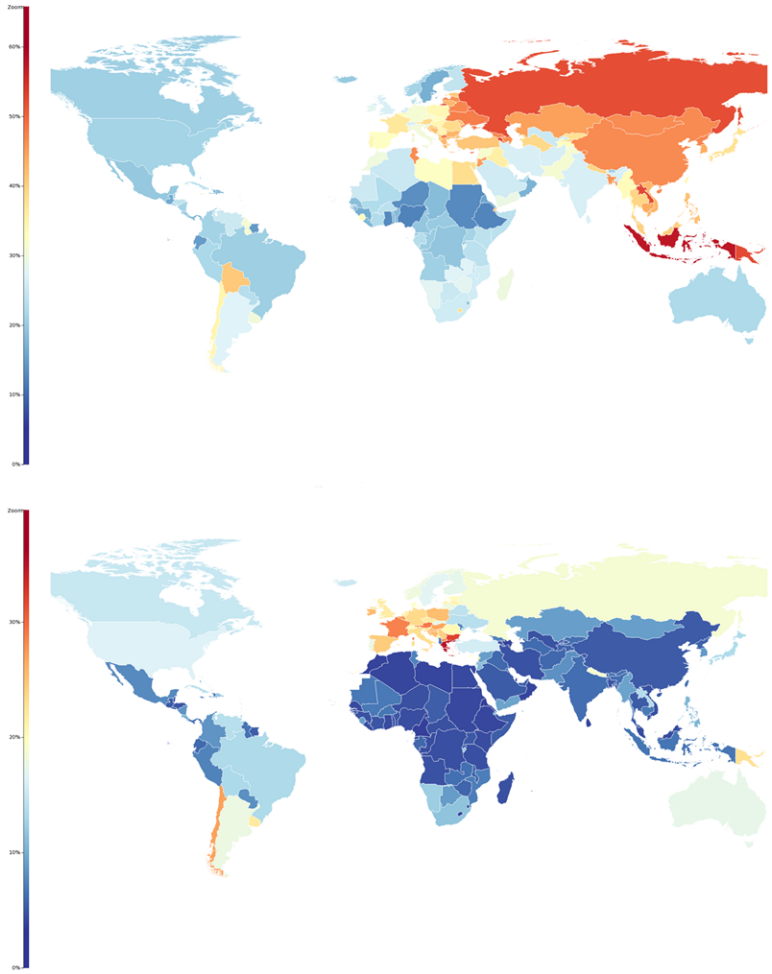

Figure 6.

Age-standardized prevalence of smoking as percent of population, males (top), females (bottom). From *JAMA.* 2014;311(2):183-192.[28]

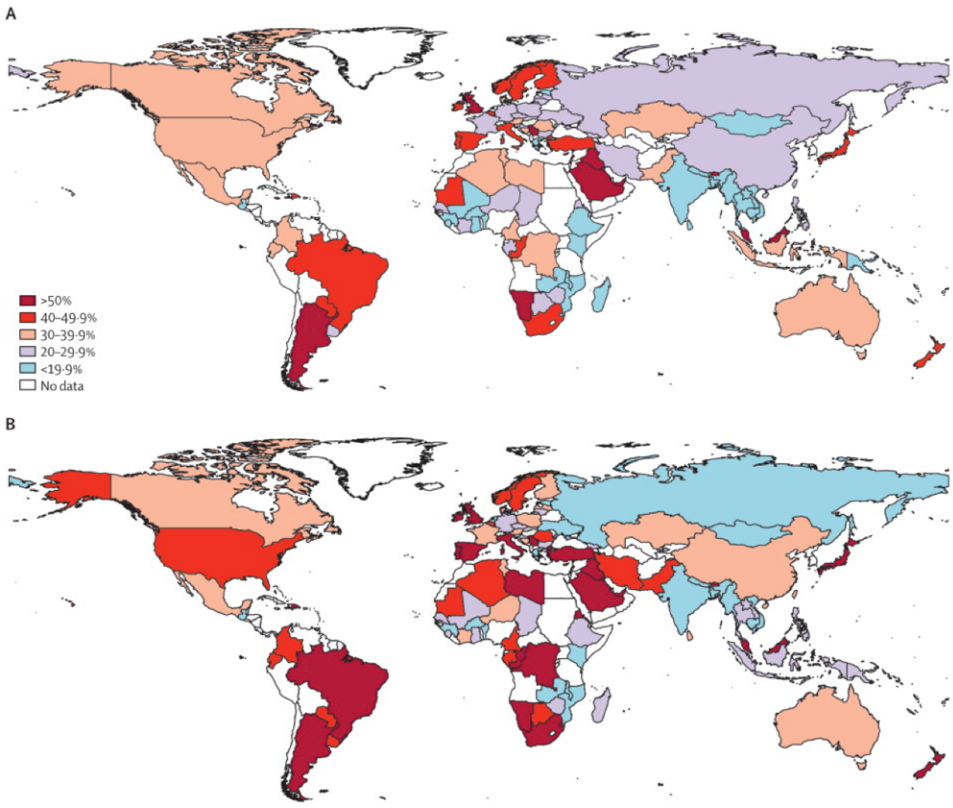

Figure 7.

Age-adjusted percent of adults who are physically inactive, males (A) and females (B). From Lancet 2012, 380(9838):247-257.[34]

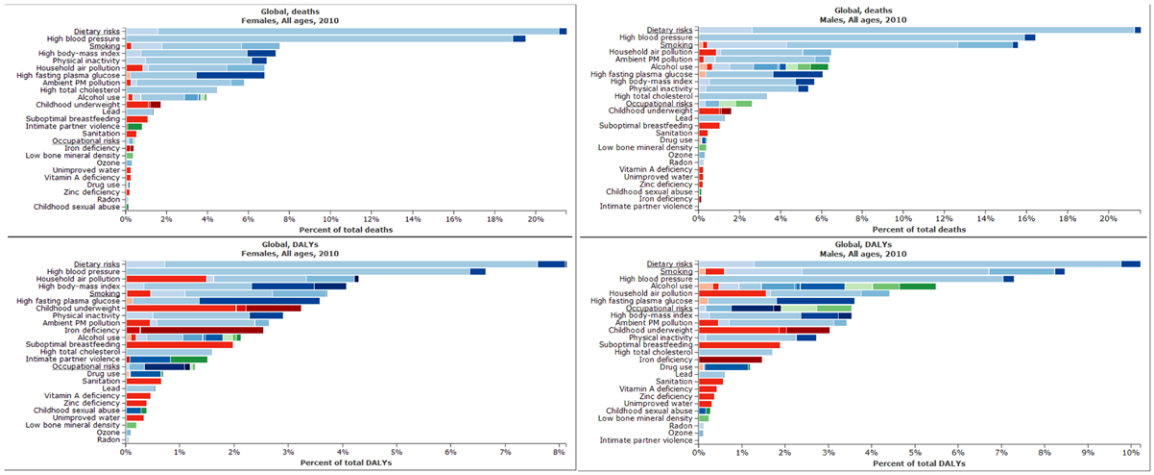

Figure 8.

Percentage of total deaths (top) and DALYs (bottom) in LMICs for males (left) and females (right) of all ages attributable to different categories of risk factors. Data from 2012 Global Burden of Disease.[206]

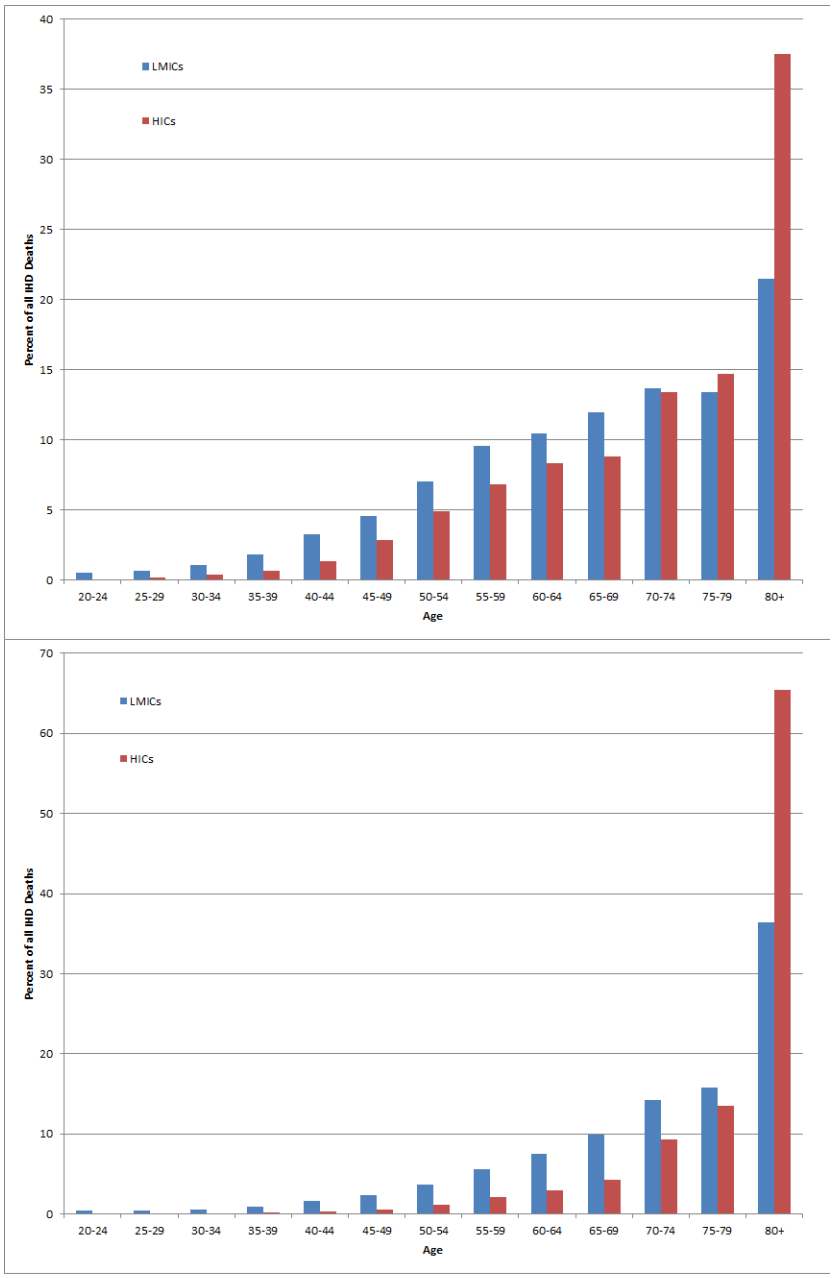

Figure 9.

Age distribution of male (top) and female (bottom) IHD (ischemic heart disease) deaths in 2010 among countries classified as high-income versus low- and middle-income. Data from 2012 Global Burden of Disease.[1]

Circ Res. Author manuscript; available in PMC 2015 June 06.

Table 1

Declines in coronary heart disease mortality in selected high- and middle-income countries, with attributable portions due to risk factor changes (prevention) and treatment.

Region	Years	Age Range	Initial CHD Mortality Rate[+]	Final CHD Mortality Rate[+]	Percent Change	Percent Attributable to Prevention	Percent Attributable to Treatment
England & Wales[207]	1981-2000	25-84	Males: ~530	Males: ~250	-53	58	42
			Females: ~180	Females: ~90	-50		
Finland[208]	1982-1997	35-64	Males: 420	Males: 150	-64.3	53-72	23
			Females: 70	Females: 20	-71		
Ireland[209]	1985-2000	25-84	8681[*]	4918[#]	-47	48.1	43.6
Italy[210]	1980-2000	25-84	Males: 267.1	Males: 141.3	-47.1	55	40
			Females: 161.3	Females: 78.8	-51.1		
Auckland, New Zealand[211]	1982-1993	All Ages	2366[*]	1808[#]	-23.6	54	46
Scotland[212]	1975-1994		21438[*]	15234[#]	-28.9	51	40
Sweden[213]	1986-2002	25-84	Males: 544.1	Males: 253.4	-53.4	55	36
			Females: 291.5	Females: 140.0	-52.0		
USA[214]	1980-2000	25-84	Males: 542.9	Males: 266.8	-50.9	44	47
			Females: 263.3	Females: 134.4	-49.0		

[+] Rates given per 100,000 population

[*] Expected number of deaths in final year with age-specific rates of initial year

[#] Observed number of deaths in final year

CHD = coronary heart disease

Table 2

Summary of published literature regarding acute coronary syndrome in low- and middle-income countries.

					In-Hospital					Discharge					
Study	**Region**	**Study Design**	**N**	**Mean Age**	**ASA**	**ACE-I/ARB**	**Statin**	**BB**	**Reperfusion**	**ASA**	**ACE-I/ARB**	**Statin**	**BB**	**F/U**	**%Morality**
ACCEPT (106)	Brazil	Registry	2,485	63	0.97	0.68	0.91	0.80	0.88*	NR	NR	NR	NR	30-Day	1.6
ACCESS (116)	Algeria, Argentina, Brazil, Colombia, Dominican Republic, Ecuador, Egypt, Guatemala, Iran, Jordan, Kuwait, Lebanon, Mexico, Morocco, Saudi Arabia, South Africa, Tunisia, United Arab Emirates, Venezuela	Registry	12,068	59.2	0.93	0.78	0.94	0.78	0.28	0.90	0.75	0.89	0.76	12 months	7.3
Aga Khan University Hospital, Nairobi (101)	Nairobi, Kenya	Registry	111	64	NR	NR	NR	NR	0.38	NR	NR	NR	NR	In-Hospital	8.1
Brazilian Registry of Acute Coronary Syndromes (RBSCA) (100)	Brazil	Registry	2,693	63	0.95	0.70	0.77	0.77	0.643	NR	NR	NR	NR	In-Hospital	5.5
BRIDGE-ACS (177)◆)	Brazil	Randomized Trial	548	62	0.958	NR	0.729	NR	NR	0.928	0.761	0.86	0.817	30-Day	8.4
CRACE (108)	China	Registry	1,301	63	0.98	0.82	0.74	0.98	0.64	NR	NR	NR	NR	In-Hospital	4
CREATE (130)	India	Registry	20,937	58	0.979**	0.568	0.52	0.59	0.104	NR	NR	NR	NR	30-Day	6.7
DEMAT (118)	India	Registry	1,565	58	0.96	NR	0.93	0.79	0.67	0.94	0.66	0.88	0.79	30-Day	2.1
Euro Heart Survey 2009 AMI Snapshot (107) ✠	Armenia, Bosnia-Herzegovinia, Bulgaria, Croatia, Czech Republic, Georgia, Hungary, Kazakhstan, Kosovo, Macedonia, Moldova, Poland, Romania, Russian Federation, Serbia and Montenegro, Slovakia, Slovenia, Ukraine	Cross-Sectional Survey	1,329	64	0.96	0.86	0.92	0.84	0.62	0.92	0.85	0.92	0.84	In-Hospital	9
Gulf RACE-2 (109)	Bahrain, Saudi Arabiam Qatar, Oman, United Arab Emirates, Yemen	Registry	7,930	57	0.98	0.76	0.95	0.74	0.18	0.93	0.78	0.91	0.79	12 months	12
Kerala ACS Registry (98)	Kerala, India	Registry	25,748	60	0.93	0.28	0.70	0.66	0.33	0.76	0.26	0.70	0.63	In-Hospital	3.9
OASIS-2 (95)	Bangladesh, China, India, Lithuania, Russia, Maldives, Slovenia, Ukraine	Registry	4,615	60.7	0.95	NR	NR	0.67	NR	NR	NR	NR	NR	24 months	9.5
PURE (119,120) ❖	Argentina, Bangladesh, Brazil, Canada, Chile, China, Colombia, India, Iran, Malaysia, Poland, Pakistan, South Africa, Sweden, Turkey, United Arab Emirates, Zimbabwe	Prospective Cohort	153,966	57	NA	NA	NA	NA	NA	0.21	0.16	0.09	0.17	NR	NR
RENASICA II (99)	Mexico	Registry	8,600	62	0.88	0.71	0.14	0.51	0.51	NR	NR	NR	NR	30-Day	10
TACSR (113)	Thailand	Registry	9,373	NR	0.95	0.63	0.80	0.62	0.37	NR	NR	NR	NR	In-Hospital	12.6

					In-Hospital					Discharge					
Study	**Region**	**Study Design**	**N**	**Mean Age**	**ASA**	**ACE-I/ARB**	**Statin**	**BB**	**Reperfusion**	**ASA**	**ACE-I/ARB**	**Statin**	**BB**	**F/U**	**%Morality**
TRACS (114)	Thailand	Registry	2,007	64	0.99	0.71	0.94	0.62	0.48	NR	NR	NR	NR	12-Months	17.7
UAE-ACS Registry (110)	United Arab Emirates	Registry	1,842	51	0.95	0.70	0.93	0.81	0.814***	0.92	0.68	0.90	0.82	In-Hospital	1.7
WHO-PREMISE (121)	Brazil, Egypt, India, Indonesia, Iran, Pakistan, Russia, Sri Lanka, Tunisia, Turkey	Cross-Sectional Survey	10,000	59	NA	NA	NA	NA	NA	0.821	0.398	0.298	0.481	NA	NA
WHO-SAGE (128)	China, Ghana, India, Mexico, Russia, South Africa	Prospective Cohort	47,443	44	NA	NA	NA	NA	NA	NR	NR	NR	NR	NR	NR

◆BRIDGE-ACS (177) data from control arm only.

ǂEuro Heart Study data from Central and Eastern regions only

❖PURE study ages for CHD only, proportions for CHD in LMICs only.

*STEMI patients only;

PCI + CABG;

**Any antiplatelet agents;

Fibrinolytics & CABG & deferred PCI;

***STEMI with LBBB patients only

NA = not applicable; NT = not reported