

The Devil Is in the Details Achieving Reductions in Global Cardiovascular Disease Mortality

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Achieving historic reductions in global cardiovascular disease (CVD) mortality will require attention to detail in 4 areas: a clear understanding of current trends in CVD mortality, an appreciation of what has influenced positive trends in CVD mortality, a knowledge of which interventions are cost-effective, and an ability to scale the interventions. Globally, CVD mortality has increased,¹ but this statistic belies significant successes that have already occurred. Although CVD mortality overall has increased, the reasons require a devil in the details look at various trends that give us this summary statistic.² First, the world population is aging in part because of our successes in managing many of the challenges of previous centuries, including improved control of infectious diseases and increased food supplies to the starving. Second, the overall world population is growing. Third, we have recently developed and implemented successful solutions to control more recent afflictions, such as HIV/AIDS.

Article see p 541

A better statistic for evaluating success than total mortality is age-adjusted mortality where we have also seen tremendous reductions in age-adjusted CVD mortality. Recent estimates suggest that age-standardized death rates because of ischemic heart disease dropped from over 200 per 100 000 to <150 per 100 000 over the last 30 years.³ Here again, a closer look suggests different trends by country within an overall global aggregate decline. In high-income countries (HICs), such as the United States and Finland, there have been dramatic declines in age-adjusted death rates from >300 per 100 000 to nearly 100 per 100 000 over the same time frame. In comparison, less dramatic declines occurred in most other countries and even increases in age-adjusted ischemic heart disease mortality occurred in some Latin American and many Eastern European countries, such as Russia.

With such varying experiences in age-adjusted mortality rates, it is essential to understand what works and what does not before adopting interventions in other countries. Previously, scientists have studied the declines in the HICs to determine

what led to such dramatic developments. Ford and Capewell used a statistical model to assess the relative contribution of cardiac treatments and changes in risk factors in reducing the burden of CVD to better understand the trend of cardiovascular deaths in the United States.⁴ Compared with deaths 2 decades before, there were ≈340 000 fewer deaths in 2000, of which 44% were attributed to reduction in risk factors (total cholesterol, systolic blood pressure, smoking prevalence, and physical inactivity) and 47% were attributed to acute management and secondary prevention (improved revascularization, treatment for acute myocardial infarction and heart failure, and other treatments).⁵ In addition to improved therapies, the development of coronary care units, where patients with high cardiovascular acuity could be monitored and managed, also contributed to the reduction in cardiovascular mortality.⁶ Similarly, there has been a 50% to 80% decline in CVD mortality in most HICs, including Canada, United Kingdom, Scotland, Sweden, and New Zealand.⁷ As seen in the United States, the 40% to 75% of the reduction in mortality in other HICs can be attributed to changes in risk factors and 25% to 50% can be attributed to more effective treatments.⁷

The reductions in risk factors have been a result of both population-based strategies and individual-level treatments. Population-level strategies include efforts, such as taxation for smoking, education about healthy diets, and physical activity, and personal interventions include such activities as screening and treatment for those identified at high risk. Both strategies can be cost-effective. Population-based interventions target high proportions of the population and may achieve modest reductions in overall risk levels.⁸ Personal interventions target smaller proportions of the population and may cost more per intervention but will achieve larger levels of absolute reductions in the targeted population. Depending on the efficiency of the intervention itself, one may be more cost-effective than the other.^{9,10}

The 3 largest drivers on what is either cost-effective or cost-saving is the risk of the population being targeted, the benefit of the intervention itself, and then obviously the cost of the intervention. Furthermore, not all interventions or prevention strategies are cost-saving. A common misperception is that prevention activities are cost-saving and interventions after the development of disease are not cost-effective. However, summary data suggest that slightly <20% of all interventions are cost-saving.¹¹ Further, those interventions that are cost-saving are evenly split between prevention and treatment services. Many other interventions are cost-effective or a good value for the expenditure, but again these seem to be evenly split between preventive services and treatment interventions.

The study by Basu et al¹² in this issue of *Circulation: Cardiovascular Quality and Outcomes* shows that a proposal

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to treat a relatively lower-risk population with inexpensive and highly effective medications can achieve an equally cost-effective result as treating a high-risk population (tertiary services) with more expensive but also highly effective services. Specifically, Basu et al examine the impact of increasing insurance coverage for cardiovascular services in India. They test in their simulation model whether it is cost-effective to provide coverage for primary, secondary, and tertiary services. Primary prevention included generic medications for those with hypertension and statins for those at high overall cardiovascular risk. Secondary prevention consisted of a combination of generic aspirin, β -blocker, angiotensin-converting enzyme inhibitor, and statin for those with a prior stroke or ischemic heart disease. Tertiary care included management of acute myocardial infarction and stroke, including potentially percutaneous coronary interventions and coronary artery bypass surgery. They found that a combination of coverage for primary, secondary, and tertiary services would be cost-effective compared with no insurance coverage of these services. The intervention combining the 3 levels of services would cost \$1331/disability-adjusted life years averted, which would be cost-effective in India using the international convention of <1 times GDP/capita as a good buy.

The results were, however, sensitive to the level of suboptimal or inappropriate care, particularly in the tertiary services. If just over 10% of individuals received inappropriate care or unnecessary procedures, then treatment for tertiary care would no longer be cost-effective. This situation is analogous to the American Heart Association/American Stroke Association recommendations regarding carotid artery stenting or endarterectomy for those with asymptomatic carotid artery stenosis.¹³ In the updated guidelines, surgery or stenting would only be recommended if the peri-procedural risk is $<3\%$.

Thus, in order for the tertiary care procedures to be recommended, local guidelines evaluating the appropriateness of procedures should also be implemented. In addition, quality of the services to ensure that the same event reductions that have occurred elsewhere should be put in place to guarantee success of the coverage for these interventions. In the other direction, improving the quality of the services will enhance the cost-effectiveness of the care delivered. Understanding what exactly are the unnecessary procedures will be important. The authors allude to unnecessary coronary artery bypass surgery procedures, but where exactly that line is drawn will need further evaluation. Furthermore, the authors assume that capacity already exists to provide the tertiary level of services. In areas where capacity is not in place for any of the services, the cost-effectiveness of the interventions will be diminished. Whether that is enough to no longer make them attractive would need to be assessed separately.

Despite successes to reduce CVD globally in many HICs, only more recently have concerted efforts been made to address this problem on a more global scale. In 2011, noncommunicable diseases were a focus of the UN General Assembly. Eight months later, the 65th World Health Assembly passed a resolution to reach a global target of 25% reduction in premature mortality from noncommunicable diseases, such as cardiovascular disease, cancer, diabetes mellitus, and

chronic respiratory diseases, by 2025.¹⁴ This historic resolution was adopted by all 194 member countries, highlighting the shared burden faced by all nations. To achieve the goal, the WHO established targets for 6 risk factors (hypertension, tobacco, sodium intake, physical inactivity, harmful alcohol intake, and obesity) and 2 health systems-based goals (better access to essential medications and technologies and drug and counseling therapy). In parallel, in 2013, the Global CVD Taskforce brought together leading organizations to address the goals, including the World Heart Federation, the American Heart Association, the American College of Cardiology, the European Society of Cardiology, European Heart Network. One of the initial actions of the Taskforce was a commitment to a 25% reduction in premature cardiovascular mortality by the year 2025.

The target seems to be reasonable given the prior evidence that the specific risk factors targeted, and access to essential medications, seem critical to success. The challenge is whether insurance coverage itself will facilitate the use of the needed services in India and other countries to achieve these goals. Initial evaluation of the natural experiment in Oregon suggests some caution.¹⁵ The state of Oregon was unable to expand Medicaid insurance to all who qualified based on income. Individuals on a waiting list were randomized through a lottery system to either Medicaid insurance coverage or no coverage. After 2 years, no significant difference was noted in the prevalence or diagnosis of hypertension or high cholesterol levels or the use of medications for these conditions, even though there was a higher proportion in the insured group who were diagnosed with diabetes mellitus and catastrophic expenditures were nearly eliminated. In contrast, other studies,^{16,17} including a recent evaluation based on propensity score matching of a national sample from the National Health and Nutrition Examination Survey, suggest that there is a positive association between insurance status and probability of being diagnosed and managed with improved indices for hypertension, hypercholesterolemia, and diabetes mellitus.¹⁸

In summary, successful efforts to reduce premature CVD mortality in low- and middle-income countries are likely to combine a mix of population and individually based interventions. Certainly, cost-effective interventions exist for both if they can be implemented with efficiency at scale. Primary and secondary prevention interventions focused on those individuals at high risk of CVD are likely to succeed if restricted to those interventions with prior proven success and delivered at low cost. Further, tertiary services must be able to be provided with high quality and appropriateness to be cost-effective. Finally, efforts at evaluating the best strategies to increase the scaling of proven interventions need to be encouraged. Insurance coverage will at a minimum lead to a reduction in catastrophic expenditures related to CVD hospitalizations. Its impact on efficient use of primary care services may need more evaluation.

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