Are We There Yet?
Steps Along the Way Toward Implementing Evidence-Based Heart Failure Guidelines in Middle-Income Countries

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In September 2011, the United Nations General Assembly met in special session, with 31 heads of state present, to discuss the growing burden of noncommunicable diseases (NCDs) globally. It was only the second time in its 66-year history that the United Nations has had a special session on a health topic. The focus of attention was on the 4 leading causes of mortality, representing >60% of all deaths globally: cardiovascular diseases (CVD), cancer, chronic respiratory diseases, and diabetes mellitus. The meeting had 3 round table discussions to focus attention on: (1) the overall health and economic burden of NCDs, (2) developing national capacity for cost-effective and sustainable prevention and treatment of NCDs, and (3) cooperation among nations toward achieving these objectives.

Although NCDs have been recognized as a significant problem in developed countries for longer than the United Nations has itself been meeting in New York, little attention has been devoted to NCDs in low- and middle-income countries. The urgency for finding solutions to the NCD burden for some regions is, however, greater for some regions than for others. In Eastern Europe and Central Asia, nearly 60% of all deaths are attributable to CVD alone, which is nearly double the rate for high-income countries.

In this issue of Circulation: Heart Failure, Hebert and colleagues report on the feasibility of a pilot disease management program for heart failure in the Tbilisi, Georgia, area. The study addresses a potentially significant problem in this region. Most deaths in the region are due to CVD, and most CVD deaths in this region are due to ischemic heart disease. Data on the prevalence of congestive heart failure are not adequately described in this region; however, given the high prevalence of ischemic heart disease and hypertension, it is likely that it is high. Thus, it is not surprising that the authors found, in the war-torn country of Georgia, that 400 of 2500 adult patients screened had reduced left ventricular function (ejection fraction [EF] <40%).

The intervention included training 2 Georgian cardiologists on how to screen, enroll, and manage patients with systolic heart failure, according to American College of Cardiology and American Heart Association (AHA) guidelines for the disease. In addition, titration schedules for medications and reviews of the cardiovascular examination were part of the training of physicians. Patients with an EF of <40%, based on portable 2D echocardiographic machines, were asked to participate in the study. Patients received free visits and testing for the 2-year study period but were responsible for their medication purchases, although the medications were dispensed directly to the patients by the study team. Patients had visits at 2-week intervals over 8 weeks to titrate medications and then were seen every 3 months. Patients also received education on smoking cessation, daily weight measurements, and a sliding scale for adjusting diuretic dosage if weight increased by >1 kg. Outcomes included self-reported medication adherence, self-reported emergency department visits and hospitalizations, and mortality. The EF and other physical measures were also recorded.

The study population, in many respects, reflects the state of care in developing regions of the world. β-Blocker treatment was <10%, and angiotensin-converting enzyme inhibitor use was <20%. A World Health Organization study revealed that only 23% and 38% of eligible CVD patients received β-blockers and angiotensin-converting enzyme inhibitor, respectively, in low-income countries. Remarkable findings from this study include the significant reduction in the systolic blood pressure of 30 mm Hg and the nearly halving in the smoking rates among the participants.

The average blood pressure decrease in this group was larger than expected. The patients were, on average, taking 2.7 medications, with 90% of them taking aspirin. Thus, on average, the patients were taking 2 blood pressure medications: a β-blocker, furosemide, or an angiotensin-converting enzyme inhibitor. A meta-analysis by Wald and Law found that patients taking 2 antihypertension medications at full dose, with a starting blood pressure of 140 to 150 mm Hg, would achieve ≈15- mm Hg reduction, with those taking 3 medications experiencing reductions close to 22 mm Hg. Whether the level of blood pressure reduction that occurred in this pilot study can be sustained for longer periods or can be repeated in other settings warrants further studies.

Regarding smoking, the patients received written and verbal counseling regarding smoking risks. A quit rate of nearly one half from this simple intervention is also greater than expected. A meta-analysis of various methods for...
smoking cessation shows, regardless of methods, that the intervention yields <10% more quitters than the control group. Because there is no control group, the potential benefits of the disease management program, in addition to general care, are unknown. However, a population-based assessment comparing self-help versus some type of external assistance revealed quit rates of 7% versus 15%. Other findings include a significant change in EF, from 31% to 36%, and improvement in New York Heart Association class, both of which would suggest mortality improvement if sustained. Visits to the hospital emergency department and hospital admissions were both reduced, but this was affected by much of the population being displaced by the war during the study period and it was based on self-reported information, which has its own limitations. Furthermore, because the study did not have a control arm, we cannot determine what effect the program had compared with usual care once heart failure was diagnosed.

The results from this study are encouraging. Conducting the study in an environment with limited resources in the middle of a war was a challenge, yet the authors showed that with a simplified protocol based on established evidence-based guidelines, heart failure can be managed effectively. However, to prevent death or morbidity from chronic diseases in an economically sustainable manner, an intervention should meet at least 4 conditions. First, the intervention must target conditions or risk factors that have been causally associated with chronic disease outcomes. Second, there should be knowledge that the intervention will likely lead to favorable changes in the outcomes or its risk factors, which should then lead to reductions in morbidity or fatal events. Third, evidence should show that the intervention is cost-effective in the settings in which it is implemented. Finally, there should be evidence that the scaling up of the intervention is fiscally feasible in resource-constrained countries.

This study met the first 2 conditions but, because of limitations of the study design, we know less about the cost-effectiveness of the intervention being able to be scaled up. The authors were unable to provide estimates of cost-effectiveness because they do not have a comparative arm of usual care to assess the added benefits and because they have self-reported information on the hospitalizations without cost-of-hospitalization data. However, we can compare the results with those of other cost-effectiveness analysis. Investigators from Texas found their congestive heart failure disease management program to result in a cost-effectiveness ratio of $43 000 per quality-adjusted life year gained. Lifetime increased costs, as the result of both the program and medical costs, were $5000; the increase in lifespan of the patients was 51 days in the program. This was based on modest improvements in New York Heart Association class that are less than what was seen in the Georgian study. The cost per quality-adjusted life year in Georgia could be <$43 000 if the additional costs were similar or less and the effects in change of New York Heart Association were as significant as reported. However, with a gross domestic product per capita of $5000, this ratio may not be acceptable. The World Health Organization and World Bank recommend interventions that are 1 times the gross domestic product per capita as a good buy and 3 times the gross domestic product per capita as an upper limit for adoption. Thus, the ratio needs to be <$5000 or <$15 000, respectively, per quality-adjusted life year to be a good or acceptable threshold for adoption, according to these recommendations. A reason why the program may not be cost-effective is that it is run only by cardiologists. Although cardiologists in Georgia likely make less than their counterparts in the United States or other western European countries, the success of other disease management programs is, in part, because of the use of other nonphysician providers with lower salaries. Other factors that influenced the effectiveness of the intervention included free care for the study participants and easy access to the medications. It is unclear what impact this may have had on the results.

Even if the intervention proved to be cost-effective, attempts to scale the program may meet significant challenges. The first challenge is whether the intervention could be maintained for a longer duration than in the trial setting. This program required 2 cardiologists to be trained both to read the echocardiograms and to be familiarized with the American College of Cardiology/AHA guidelines for managing heart failure. Physician shortages are great worldwide. In some countries, the ratio of physicians per population is one tenth to one hundredth that of high-income countries. Even scarcer are specialists. Many health functions are managed by nurses, and it is unclear if this disease management program could be implemented without cardiologists to diagnose and manage the program if nurses would achieve the same results. However, at least some features of the program could be managed by other health professionals. Studies suggest that nurses could manage hypertension as well as physicians, but it is unclear if the result would be the same in this more detailed regimen of advancing medications for heart failure than managing essential hypertension. Other study components that may limit scale up include access to echo machines for diagnoses and follow-up and lack of adequate general health insurance coverage. With ≤70% of Georgians failing to access care because of affordability, sustainability of the program could be significantly hampered.

Hebert and colleagues have advanced along several of the steps required in translating knowledge from high- to low- and middle-income countries. First, they have acknowledged the cultural and economic conditions of their host country environment in designing the program. Second, they have tested and proved that a set of guidelines that were simplified given the conditions available in Georgia can lead to significant improvements in physiological parameters and patient quality of life for heart failure patients using standard generic medications. However, before widespread adoption in Georgia or other low- and middle-income countries, assessments of their cost-effectiveness and feasibility for widespread adoption will need to be evaluated.

Disclosures
None.

References


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