

# Is a multidrug regimen cost-effective for the prevention of cardiovascular disease in resource-poor countries?

**Original article** Gaziano TA *et al.* (2006) Cardiovascular disease prevention with a multidrug regimen in the developing world: a cost-effectiveness analysis. *Lancet* 368: 679–686

## SYNOPSIS

**KEYWORDS** cardiovascular disease, cost-effectiveness, developing countries, prevention

### BACKGROUND

Cardiovascular disease (CVD) is an increasing problem in the developing world, yet health-care budgets in these countries are low and resources limited. Drugs proven effective for the prevention of CVD are available but typically underused in low-resource settings, partly because of the preconception that these treatments are expensive.

### OBJECTIVE

To assess the cost-effectiveness of four generic drugs for primary and secondary prevention of CVD in the developing world.

### DESIGN

The authors designed a Markov model to investigate the benefits and cost-effectiveness of two regimens combining four drugs recommended by the WHO for the prevention of CVD. The first regimen was used for primary prevention in patients with no history of CVD and comprised 81 mg aspirin, 40 mg lovastatin, 10 mg lisinopril, and 5 mg amlodipine. The second regimen, for secondary prevention in patients with previous CVD, was identical but for the substitution of metoprolol for amlodipine. These two combinations were tested in six settings; for primary prevention, the first regimen was used for patients aged older than 55 years, and those with an absolute risk of cardiovascular events of 5%, 15%, 25%, or 35% over a 10-year period. Additional costs in these five groups were outpatient visits, measuring blood pressure and cholesterol levels, and testing for diabetes. For secondary

prevention, the second regimen was used and no additional costs were involved. These five strategies were compared across the six low and middle-income areas defined by the World Bank (East Asia and the Pacific, Eastern Europe and Central Asia, Latin American and the Caribbean, Middle East and North Africa, South Asia, and sub-Saharan Africa).

### OUTCOME MEASURES

Outcome was evaluated by calculating quality-adjusted life years (QALY) gained and net health-care expenditure. For comparison, incremental cost-effectiveness ratios (ICERs; the difference in cost divided by the difference in QALY) were calculated for each strategy in each of the six regions.

### RESULTS

The model predicted that the lifetime risk of death from CVD in individuals aged between 34 and 74 years was 22–40%. With primary prevention, this lifetime risk decreased across the six regions to 15–28%, 12–25%, and 9–23% in individuals with a 10-year risk of >25%, >15%, and >5%, respectively. Lifetime risk also decreased to 20–34% with the secondary prevention strategy. For primary prevention, the ICER was US\$746–890/QALY gained, \$790–930/QALY, and \$1,039–1,221/QALY for individuals with a 10-year absolute risk of CVD of >25%, >15%, and >5%, respectively. For the secondary prevention strategy, the ICER was \$306–388/QALY gained. For each of the six strategies, the ICER for each region was less than three times the gross national income per head for that region (the measure of cost-effectiveness used by the WHO).

### CONCLUSION

Both drug combinations are cost-effective in each of the six geographical regions and could potentially halve the risk of death from CVD in the developing world.

## COMMENTARY

## K Srinath Reddy

CVD is not only the leading cause of global mortality, but is also becoming the principal contributor to death and disability in many low and middle-income countries. Large populations mean that these countries already account for 80% of global CVD deaths<sup>1</sup> and proportional mortality is also rising rapidly. The economic costs of neglected CVDs are very high in terms of potentially productive years of life lost.<sup>2</sup> These countries can ill afford to lose human resources because of mid-life CVD or expend scarce financial assets on costly clinical care of the growing multitudes of CVD patients.

The advancing CVD epidemic calls for a comprehensive public-health response that will integrate population-wide interventions to prevent risk acquisition with cost-effective interventions for risk detection, stratification and reduction among individuals.<sup>3</sup> Primary prevention poses challenges, both in terms of screening and providing effective treatments at affordable cost. Secondary prevention is easier in terms of identifying individuals who would benefit, but still needs to be used more widely to attain its full potential. Angiotensin-converting-enzyme inhibitors and statins are reported to be used by fewer than 20% and 10%, respectively, of those who need secondary prevention of CVD in resource-poor countries.<sup>4</sup>

The paper by Gaziano *et al.* highlights the need for a wider and more-effective application of pharmacologic interventions of proven life-saving value for primary and secondary prevention of CVD in the developing world. Although this plea has previously been made by others, this paper makes the argument more robust by presenting well-conducted economic analyses of the QALY gained through the use of multidrug regimens.

The efficacy of the multidrug regimens recommended by Gaziano *et al.* is well supported by recent trial data. The absolute risk thresholds for such multidrug therapy, in the case of primary prevention, would need to be guided by the cost-effectiveness estimated for each risk threshold and the feasibility of implementing such a program, based on available national resources. While cost-effectiveness of such treatments is

indicated by the modeled estimates of this study, these multidrug regimens could remain largely unaffordable in many low-income countries, particularly if resource-constrained governments have to choose among competing options across several diseases. The safety of multidrug combinations also needs to be evaluated in primary prevention scenarios, although trials of secondary prevention have often employed these drugs in combination, to test incremental benefit, without major adverse effects.

Current interest in the 'polypill' or 'combination pill' also adds further relevance to this paper.<sup>5</sup> Gaziano *et al.* contend that the polypill, while theoretically attractive, has yet to prove its merits in terms of efficacy, safety and improved adherence in clinical trials. They argue that there is currently an urgent need to use multidrug therapy to provide appropriate and affordable care to the large numbers of people who are at high risk of CVD and who would benefit immensely from such intervention.

Although the case is well made, strong advocacy is needed for these recommendations to be transformed into policy and translated into programs in the developing world. Policymakers and health professionals both need to be educated about the benefits of timely risk-reduction, so that missed opportunities in routine practice are minimized. Essentially, the prevention of CVD should integrate population-based programs for averting risk acquisition and pharmacotherapy to reduce elevated risk.

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## Competing interests

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## PRACTICE POINT

Combination regimens of drugs of proven efficacy are likely to be quite cost-effective for CVD prevention in high-risk individuals in low-income countries and should be prescribed wherever possible