Economic Evaluation of Primary Prevention of Cardiovascular Diseases in Mild Hypertension: A Scenario Analysis for the Netherlands

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ABSTRACT

Background: In the Netherlands, antihypertensive treatment for patients with mild hypertension is recommended if the 10-year cardiovascular disease (CVD) risk exceeds 20%. Recent evidence suggests that lifelong CVD risk estimates might be more informative than 10-year ones. In addition, the cost of antihypertensive treatment in the Netherlands has decreased during the last decade.

Objective: The aim of this study is to estimate the cost-effectiveness of lowering systolic blood pressure (SBP) in patients ineligible for treatment in both a 10-year and a lifetime horizon.

Methods: A Markov model was developed to assess the cost-effectiveness of SBP reduction compared with no reduction in patients with mild hypertension and low CVD risk. Modified SCORE (Systematic Coronary Risk Evaluation) risk estimates were used to predict fatal and nonfatal CVD events. We analyzed scenarios for different age groups, sexes, and SBP reductions. Specifically, SBP reductions due to hydrochlorothiazide (HCT) 25 mg and hypothetical reductions with HCT 12.5 mg-losartan 50 mg combination were assumed. Parameter uncertainty was assessed through a probabilistic sensitivity analysis.

Results: In a 10-year horizon, in scenarios of SBP reduction with HCT 25 mg, the incremental cost-effectiveness ratio (ICER) estimates for men varied across different ages in the range of €6032 to €58,217 per life-year gained, whereas for women ICER estimates were in the range of €12,345 to €361,064 per life-year gained. In a lifetime horizon, the cost-effectiveness estimates were favorable for both sexes. In scenarios of hypothetical SBP reductions, more favorable ICER estimates compared with no reduction were found. A large uncertainty around the cost-effectiveness estimates was observed among all scenarios.

Conclusion: Larger SBP reductions were found to be cost-effective in both a 10-year and lifetime horizon. These findings might call for more aggressive SBP reductions in patients with mild hypertension. However, a high level of uncertainty surrounds these cost-effectiveness estimates because they are based on CVD risk prediction modeling. (*Clin Ther.* 2014;36:368–384)

Key words: cardiovascular diseases, cost-effectiveness, hypertension, prevention.

INTRODUCTION

Cardiovascular disease (CVD) is the largest cause of morbidity and a major cause of premature death and reduced quality of life in Europe. At the same time, CVD is the most significant contributor to health care expenditures; treatment costs of CVD in the European Union comprise 12% of all health care costs (€105

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billion),[1] whereas in the Netherlands they reach 8% of the total health care budget (€5.5 billion).[2]

Because people with moderate or high hypertension (blood pressure, >160 mm Hg), previous CVD events, or diabetes mellitus (DM) are generally considered to be at higher risk for CVD, preventive treatment in these groups is rather straightforward and common.[3,4] The question arises when considering preventive treatment in patients with mild hypertension (blood pressure, 140-160 mm Hg), no prior CVD events or DM, and overall low CVD risk,[4] given the economic implications and ethical considerations of such a decision. Currently, national guidelines recommend lifestyle changes as a first step in lowering blood pressure in this patient population.[5] Failure of this intervention should be followed initially with diuretic treatment (eg, hydrochlorothiazide [HCT]) and if necessary combinations of diuretic and angiotensin-converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB).[5] In parallel, the cost of these antihypertensive agents has decreased considerably the last years in the Netherlands, primarily due to generic introduction,[6] causing a reduction in the cost of treating patients with hypertension. Guideline recommendations on preventive treatment of CVD in people with neither prior events nor DM necessitate the estimation of a patient-specific risk for fatal or nonfatal CVD.[3–5,7–9] Several studies have focused on identifying and correcting for risk modifiers (eg, reducing systolic blood pressure [SBP] or cholesterol level) that can be beneficial for cardiovascular risk reduction.[10–15] Considering the overall prevalence of hypertension and the fact that elevated SBP is a major cardiovascular risk factor, considerable health and economic benefits are expected from its control.[16–19]

The effective control of SBP through antihypertensive medication has been established through numerous clinical trials.[20] However, the effectiveness of these drugs often varies across trials. Under these circumstances, the proper consideration of the exact long-term health and economic consequences of SBP reduction in patients with mild hypertension and no prior CVD events requires evidence-synthesized estimates of SBP reduction (eg, through meta-analysis and mixed-treatment comparisons).[21,22] Such estimates are currently available only for older antihypertensive agents, such as diuretics,[20] but not for newer antihypertensive agents, such as ACEIs and ARBs.

The aim of this study is to estimate the health effects and economic consequences of SBP reduction through antihypertensive treatment in patients with mild hypertension but with no history of CVD or DM. Reduction in SBP was used as a surrogate end point that was expected to, consequently, result in a CVD risk reduction. Because we are primarily interested in the effect of such an intervention in the Dutch setting, we used a CVD risk calculation model recently validated for this population (ie, the low-risk version of SCORE [Systematic Coronary Risk Evaluation]).[23,24] Furthermore, we applied cost estimates for cardiovascular complications and drug costs that reflect the Dutch situation. We investigated the cost-effectiveness of different scenarios of SBP reductions achieved by antihypertensive treatment in different age groups of men and women compared with no treatment in both a 10-year and a lifetime horizon.

METHODS

Model Structure

A Markov model was developed to compare the long-term costs and health benefits of primary CVD prevention through SBP reduction. The model included 5 health states: baseline (healthy with mild hypertension but no CVD history), acute nonfatal CVD, stable nonfatal CVD, fatal CVD, and non–CVD-related death (**Figure 1**). Patients remained in the baseline state until a fatal or nonfatal CVD event occurred or they died from other, non–CVD-related, causes. From the acute CVD state at the end of one cycle, patients could move to a stable nonfatal CVD state, experience a subsequent fatal or nonfatal CVD event, or die of other causes. From the stable CVD state, patients could experience a subsequent fatal or nonfatal CVD event or die of other causes. The model allows for multiple recurrent nonfatal CVD events to occur with a restriction to one event per cycle. Transition probabilities among health states were modeled through reparameterizing the 10-year risks of CVD mortality and morbidity and non–CVD-related mortality into respective 1-year probabilities (see **Supplemental Appendix** in the online version at 10.1016/j.clinthera.2014.01.008).

The simulations were run using 2 time horizons, 10 year and lifetime, both applying cycles of 1 year in the Markov model. All patients were assumed to be dead by the age of 100 years. The model was developed using the statistical software R (version 3.0.2).[25]