

## Original Research

# A Short-Term Cost-Effectiveness Analysis of Hypertension Treatment in Greece

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**Introduction:** Hypertension represents one of the major contributors to the disease burden and to healthcare expenditure internationally. The objective of this paper was to conduct a short term cost-effectiveness analysis of hypertension treatment vs. a hypothetical “no-treatment” strategy in Greece.

**Methods:** Health-resource use data and clinical outcomes for a cohort of 1453 hypertensive patients in Greece who were prospectively followed for a 1-year period served as the primary data for the analysis. Based on these data, the incremental cost per mmHg lowering in the baseline blood pressure (BP) and the incremental cost per patient that achieved BP control after 1 year of treatment were estimated. Costs were calculated from a social security perspective and are reported in year 2011 values.

**Results:** The average cost per mmHg lowering of baseline BP for the whole study sample was €13.7 ± 14.2, ranging from €20.3 ± 21.4 for Grade 1 hypertension patients to €9.9 ± 4.4 for Grade 3. The average cost per patient that achieved control after 1 year of treatment was €603.1 ± 215, with a range from €496.1 ± 186.6 to €868 ± 258.2 for Grades 1 and 3 baseline BP, respectively. The sensitivity analysis corroborated the results.

**Conclusions:** The present study outcomes compare favorably to corresponding results from the international literature and indicate the clinico-economic value of hypertension treatment in Greece, especially to those that are severely ill. In light of the current financial situation, resource allocation based on evidence from economic evaluation can constitute a core input in the decision-making process for health policy.

**H**ypertension is generally acknowledged as one of the primary contributors to the international burden of disease.<sup>1</sup> Taking into account that suboptimal blood pressure (BP) is the underlying cause of 49% of cases of ischemic heart disease and 62% of stroke cases occurring each year globally<sup>2</sup> and that at the turn of the millennium 26.4% of the global population was estimated to have elevated BP,<sup>3</sup> 6 million lives and 56 million disability-adjusted life years are lost every year as a result of the disease.

In this respect, Greece is no excep-

tion: approximately 40% of the adult population suffers from hypertension,<sup>4</sup> a significant proportion of whom are unaware of and, consequently, not appropriately treated for their condition.<sup>5</sup> Hypertension currently accounts for 25% of the total deaths in the country, whereas cerebrovascular and ischemic heart diseases are responsible for 17.4% of the total burden of disease.<sup>6,7</sup>

The developments of the last 50 years in the pharmaceutical armamentarium against hypertension have brought significant reductions in cardiovascular mor-

idity and mortality among hypertensive patients.<sup>8,9</sup> Nevertheless, the current (and future) obligation of health care systems to operate under severe financial constraints necessitates the use of not only clinical effectiveness but also economical efficiency data associated with each treatment option. In this light, a large number of economic evaluations comparing the incremental costs and effects between different classes of drugs,<sup>10,11</sup> or among newer and older agents of the same therapeutic class,<sup>12</sup> have been published. Complementing these analyses and extending to a higher level of resource allocation, that of the allocation of resources between diseases, a number of economic evaluations of hypertension treatment *as a whole*, i.e. as an intervention or policy choice of a health/insurance system, have been reported. These include a number of seminal economic evaluations published in the early nineties,<sup>13-18</sup> as well as newer publications.<sup>19,20</sup> Recently, cost-utility results for hypertension treatment have also been reported for Greece.<sup>21</sup>

Almost all of the aforementioned studies have concluded that hypertension treatment represents an intervention that is associated with extremely favorable cost-effectiveness ratios.<sup>22</sup> In most cases, the study methodology involved obtaining a wide time-frame of analysis (usually >20 years) and basing the outcomes on a “cost per quality adjusted life year gained” ratio. However, some authors suggest that in order to acquire a “full picture” of the economics of hypertension treatment, those data should also be accompanied by clinically meaningful cost-effectiveness evidence, such as the cost per patient of achieving BP control (indicatively<sup>23,24</sup>) or the cost per mmHg reduction in the systolic or diastolic BP.<sup>25,26</sup>

In light of the above, and in order to contribute to this discussion, the purpose of the present study was to perform a cost-effectiveness analysis of hypertension treatment in Greece, regardless of the agent(s) used, versus a hypothetical “no treatment” strategy, following a short-term time horizon and applying the costs to clinically meaningful endpoints.

## Methods

### Baseline population

The baseline population of the analysis was based on the participants in a multipoint prospective observational study on hypertension treatment in Greece. Recruitment of patients was carried out via 76 data collection points (physicians) geographically dis-

tributed throughout the country. Inclusion criteria were age 30-75 years, diagnosis of primary hypertension, and written consent to participation in the study. Patients with a recent cardiovascular episode (<1 year), known or suspected secondary hypertension, or pregnancy were excluded from the study. Patients were followed for 1 year after inclusion, a period during which patient demographics, disease parameters, such as blood pressure, cholesterol level and smoking status, as well as health resource use attributable to hypertension treatment and follow up (pharmaceuticals, consultations, lab tests, hospitalizations) were documented. Eligible treatments were all hypertension treatments administered according to the physician’s judgment, and the analysis focused on patients who were not already receiving treatment at the baseline visit. All relevant legal and ethical considerations were followed throughout the study period.

The sample initially consisted of 1511 participants, (47.17% male, average age  $59.5 \pm 9.9$  years, average baseline systolic blood pressure  $164.9 \pm 14$  mmHg), of whom 1453 completed follow up and were eventually included in the analysis. Patients were classified according to their grade of hypertension (Grade 1-3 and isolated systolic BP),<sup>27</sup> based on their baseline BP. For each group the difference between systolic BP at the beginning and at the end of the study period was recorded. Controlled patients were those that achieved BP <140/90 mmHg by the end of the study period.

### Cost calculations

The analysis was performed from a third-party payer perspective (Social Security system); thus, it considered only direct medical costs associated with treatment and patient follow up. Costs of hypertension treatment and monitoring were calculated by applying the official social security tariffs and medication costs to the health-resource use data of the cohort under survey (micro-costing). Costs of hospitalizations to a general ward or the ICU were taken from the literature.<sup>28,29</sup> Discounting of costs was not deemed necessary in view of the short time period of the analysis. Health resource use data and corresponding unit prices are presented in Table 1.

### Study outcomes

The primary outcomes of the study were the incremental cost effectiveness ratios (ICERs) of treatment

**Table 1.** Health resource use and unit costs for the treated cohort.

Resource	Average annual use (per patient)	Unit cost (€)
Lab tests:	2.00	4.75
Total cholesterol		
Blood glucose	1.23	2.22
Creatinine	1.15	4.05
High-density lipoprotein cholesterol	1.71	4.75
Low-density lipoprotein cholesterol	1.70	4.75
Hematocrit	1.64	1.76
Blood urea	1.16	2.26
Physician consultations	4.23	20/10*
Hospitalization:		
General ward	0.31	425.4
Intensive Care Unit	0.02	1786.4

\*€20 for the first and €10 for subsequent visits according to the official price catalogue

vs. a hypothetical no-treatment strategy. In general, an ICER reports the ratio of the difference in the costs of two interventions ( $Cost_{treatment} - Cost_{no-treatment}$ ) divided by the difference in the respective clinical outcomes ( $Outcome_{treatment} - Outcome_{no-treatment}$ ). In the present study, the ICERs assumed the form of (a) the *cost per mmHg lowering* in systolic BP (SBP) for treatment vs. no treatment, i.e. the difference in the average per patient cost in the respective groups of patients divided by the difference in the average BP measurements, for each stratum, and (b) the *cost per patient who achieved the BP target* for treatment vs. no treatment, i.e. the difference in costs between the two groups of patients divided by the number of patients who achieved BP control, for each stratum. The analysis followed the conservative approach that a patient with no treatment would have the same BP throughout the study year and would require the same hospitalization costs as their treated peer.

To further enhance the outcomes of the study, the average cost effectiveness ratios (ACERs) were

also calculated for treated patients. An ACER is calculated as the ratio of the costs of treatment ( $Ct$ ) divided by the respective outcomes ( $Et$ )<sup>30</sup> of an intervention:

$$ACER = Ct/Et$$

In this case, the ACERs were calculated as the cost per mmHg lowering of BP and the cost per patient who achieved BP for those under treatment.

### Sensitivity analyses

To test the robustness of outcomes, a series of one-way sensitivity analyses were performed. For that purpose, the ICERs for the total study population were recalculated based on a change of  $\pm 10\%$  in the original baseline parameter values.<sup>31</sup>

### Results

The average SBP after 1 year of treatment for the whole sample population was  $132.17 \pm 10.18$  mmHg. Of the 1453 patients who completed the one-year follow up, 1079 finally achieved the BP target. Overall, the average 1-year incremental cost between treated and non-treated patients was estimated at €446.7. Disaggregated results according to grade of hypertension are presented in Table 2.

Taking into account the difference in the costs of treated vs. non-treated patients (incremental cost) and the respective clinical outcomes, the results of the cost-effectiveness analysis are presented in Table 3. The cost per mmHg reduction in SBP tended to fall as baseline BP rose, probably as a result of a higher absolute difference between initial and desired BP, according to treatment targets. In contrast, the cost per patient who achieved control of BP rose steeply with the baseline BP levels, especially for Grade 3 patients. This could be attributed to a more intense disease management pattern for those who are more

**Table 2.** Average reduction in SBP, percentages of patients achieving BP targets and incremental costs, according to disease severity.

Classification of hypertension	N (t=0)	Average reduction in SBP (mmHg)	Patients achieving target BP [N (%)]	Incremental cost (€) (treated-non treated)
Grade 1 (SBP 140-159 mmHg and/or DBP 90-99 mmHg)	359	20.5	302 (84.1%)	417.3
Grade 2 (SBP 160-179 mmHg and/or DBP 100-109 mmHg)	636	33.3	477 (75.0%)	439.4
Grade 3 (SBP $\geq 180$ mmHg and/or DBP $\geq 110$ mmHg)	247	51.7	145 (58.7%)	509.5
Isolated systolic (SBP $\geq 140$ mmHg and DBP $< 90$ mmHg)	211	29.3	155 (73.4%)	450.8
All patients	1453	32.6	1079 (74.2%)	446.7

SBP – systolic blood pressure; DBP – diastolic blood pressure. Average reduction in SBP is the average difference in SBP between t=52 weeks and t=0.

**Table 3.** Incremental cost-effectiveness ratios of hypertension treatment (treated vs. non-treated patients).

Classification of hypertension	Incremental cost-effectiveness ratios	
	Cost (€)/mmHg	Cost (€) / controlled patient
Grade 1	20.3 ± 21.4	496.1 ± 186.6
Grade 2	13.1 ± 7.6	585.8 ± 210.3
Grade 3	9.9 ± 4.4	868.0 ± 258.2
Isolated systolic	15.4 ± 16.6	616.6 ± 213.4
All patients	13.7 ± 14.2	603.1 ± 215.0

severely ill, and the subsequent higher costs of treatment.

The ACERs of treatment, calculated after the addition of annual hospitalization costs (€173.5, €211.4, €419.5 and €181.6, for Grades 1-3 and isolated SBP patients, respectively) to the costs of treatment and monitoring, are presented in Table 4.

### Sensitivity analysis

The results of the sensitivity analysis presented in Table 5 indicated that clinical endpoints were the parameters with the biggest influence on the cost-effectiveness results. A 10% change in the absolute reduction in SBP after 1 year of treatment was the

**Table 4.** Average cost-effectiveness ratios of hypertension treatment.

Classification of hypertension	Average cost-effectiveness ratios	
	Cost (€) /mmHg	Cost (€) / controlled patient
Grade 1	27.4 ± 38.0	669.6 ± 890.2
Grade 2	17.9 ± 28.9	797.1 ± 623.9
Grade 3	14.7 ± 25.5	1287.5 ± 903.7
Isolated systolic	19.9 ± 45.2	798.3 ± 572.9
All patients	18.8 ± 33.8	827.5 ± 725.1

**Table 5.** One-way sensitivity analysis results.

Baseline parameter	Incremental cost per mmHg (all patients)		Incremental cost per "regulated" patient (all patients)	
	+10%	-10%	+10%	-10%
Cost of physician visits	13.8	13.6	609.3	598.1
Frequency of lab tests (all)	13.9	13.5	612.5	595.7
Medication prices	14.7	12.7	646.8	559.3
Absolute reduction in SBP (all patients equally)	12.5	15.3	502.5	704.4
% of patients achieving regulation (all groups equally)	-	-	548.2	670.1

+10% or -10% represents the change from the base-case scenario value.  
SBP – systolic blood pressure.

most influential parameter, imposing a >10% corresponding change in the ICERs of the analysis, as a result of both the absolute reductions in BP and the increase in the numbers of patients that achieved control of BP. The percentage of controlled patients was also examined separately and was found to have an analogous impact on the ICERs to the change in the base-case scenario value. Cost parameters, such as the costs of physician visits or the costs of medication, had a smaller effect on the ICERs.

### Discussion

Economic evaluation evidence for major health policy and public health interventions, such as hypertension treatment, is extremely valuable for demonstrating whether expenditure by organized health systems on these interventions represents "money well spent." It can also help to justify whether more or fewer of the scarce healthcare resources should be allocated for this purpose.

In principal, for a chronic disease like hypertension, economic evaluations are nowadays performed by adopting a wide timeframe for the analysis, in order to include all future aspects (costs and outcomes) of the disease/intervention under survey. The authors of this paper have presented corresponding results for hypertension treatment in Greece elsewhere.<sup>21</sup> However, to complete the economic evaluation data surrounding treatment, short term economic evaluations with clinical endpoints are necessary,<sup>23,25</sup> although sparsely reported in the literature.

Following this line of thought, and based on Greek-specific observational data, we conducted a cost-effectiveness analysis of hypertension treatment vs. a hypothetical no-treatment strategy, focusing on clinical endpoints and retaining a 1-year time horizon. The results of the analysis indicated that: (a) the

incremental (excess) cost for a patient to achieve BP control is estimated to be €603.1 on average, varying according to disease severity (higher for the severely ill), and (b) the incremental cost required for a 1 mmHg reduction in SBP is €13.7 on average, also heavily influenced by baseline BP (lower for Grade 3 patients and higher for Grade 1).

In line with the long term cost-utility results of hypertension treatment,<sup>21</sup> the outcomes of the short term cost-effectiveness analysis presented here indicate that severely ill patients could be a priority group in terms of treatment administration. The cost/mmHg ratio, i.e. the economic efficiency of treatment in those patients is substantially lower compared to less severely ill patients, given that the BP lowering margin is wider. Consequently, given the almost linear relationship between BP and the occurrence of cardiovascular events,<sup>32</sup> the projected future clinical and economic benefits from reduced mortality are higher.

The results of the present analysis compare favorably against published evidence (though limited in quantity) from the literature. Indicatively, the mean incremental cost per patient achieving BP control with treatment, reported here for the Greek healthcare setting (€603.1) is substantially lower than the respective figures (\$2704-4325 or €1931-3089) for the US setting,<sup>23</sup> or the corresponding calculations in Norway.<sup>33</sup> In the same context, a recent (2011) study of patients treated with angiotensin-receptor blockers in the UK<sup>34</sup> reported an even lower cost per patient who achieved target BP, estimated at £171-189. This cost, however, referred to medication expenditure only, as well as to a higher BP target (150 mmHg), which was achieved by 94.3% of the participating patients. In general, when the analysis focuses solely on medication costs the ICERs are highly variable, depending on the medication category that is administered.<sup>35,36</sup>

With regard to the costs per mmHg reduction in BP, to the best of our information the only study reporting similar data is that of Anderson et al,<sup>24</sup> who evaluated the use of a combination of felodipine and metoprolol versus enalapril in Sweden. The authors concluded that the ACERs (cost per mmHg lowering of BP, including expenses for medication and follow up) ranged from €26.12-43.27 for an 8-week treatment period (values adjusted to year 2011), i.e. rather higher than the figures reported by the present study.

As with any study of this kind, the present one has some limitations that should be acknowledged. First of all, the analysis was undertaken from a third-

party payer perspective; thus, it does not include costs to society, mainly the productivity losses as a result of the disease and the costs of informal care. The latter constitute an important cost variable, especially for patients whose daily activities are severely impaired by the disease. Indicatively, informal care costs can account for up to 21% or 25% of total cost for patients who have suffered a cerebrovascular or coronary heart disease episode, respectively.<sup>37,38</sup> Had the above mentioned costs been incorporated in the analysis, the cost-effectiveness ratios would probably be higher. However, this picture would be radically different in the long run, as the effects of reduced morbidity as a result of hypertension treatment would also “translate” to a sum of informal care costs that would be avoided with treatment. Thus, the cost-effectiveness results would become even more favorable (lower) for treatment, as previously demonstrated by published studies of the same kind.<sup>39,40</sup> Secondly, the baseline population of the analysis consists of patients who spontaneously visited their physician, so it is likely that their BP may have been higher than the general population average (the latter including “asymptomatic” patients). Nevertheless, the results are highly applicable to those who seek treatment and provide insight into the value of treatment to those patients. Thirdly, it should be acknowledged that 20% of hypertensive patients are affected by sleep apnea, a cause of secondary hypertension but also a bystander of essential hypertension.<sup>41</sup> The population with sleep apnea includes patients who are using CPAP therapy for both sleep apnea and hypertension. This cost was not included in the calculations given the lack of relevant data. Finally, it should be noted that the clinical endpoints of the study and, in particular the rate of control of BP, although in line with previous studies,<sup>5</sup> appear to be higher than the ones reported from more recent data.<sup>4,42</sup> This fact, according to empirical data, can be attributed to the positive influence induced by the acknowledged participation of patients in the observational trial and the subsequent enhanced adherence to treatment.<sup>43,44</sup> To account for this uncertainty, whose extent is very difficult to quantify for our study population, extensive sensitivity analyses were performed that corroborated the robustness of outcomes.

Economic evaluation cannot provide a solution to all health care policy issues. However it does represent a significant input to the decision making process,<sup>45</sup> the latter including a series of health-related and societal values that should be taken into account

in the context of resource allocation. Cost-effectiveness analysis can provide evidence-based answers as to whether the healthcare expenditures of societal welfare structures, such as social insurance funds, are merely expenditures or actually *investments* from a clinical and economic point of view. In the case of hypertension, one of the most prevalent diseases/risk factors that is accompanied by large scale costs, the above analysis demonstrated that hypertension treatment in Greece is accompanied by favorable results that could argue for further support of this intervention by the third party payers.

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