

Cost Effectiveness of Intensive Treatment of Hypertension

Based on presentations by Donald S. Shepard, PhD; and Dominic Hodgkin, PhD

Presentation Summary

The Hypertension Optimal Treatment (HOT) study showed that substantial reductions in blood pressure and a corresponding lowering of the risk of myocardial infarction could be achieved by intensive antihypertensive therapy. A cost-effectiveness analysis was performed to determine the possible economic consequences of three different targets of diastolic blood pressure lowering— ≤ 90 mm Hg, ≤ 85 mm Hg, and ≤ 80 mm Hg, and of the coadministration of aspirin.

The cost of each drug was first estimated at high and low dosage. Next, by drawing on data from the HOT trial, the mixture and dosage of drugs for each level of blood pressure control were estimated. This allowed computation of the annual cost of drugs for each blood pressure target.

Because the rate of myocardial infarction (MI) was the only end-

point that differed significantly among the three target blood pressure groups, the MI risk data were converted into years of life gained on the basis of fatalities from MI averted. The cost-effectiveness ratios, expressed as cost per year of life gained, were most favorable for the ≤ 90 -mm Hg treatment target group (\$4262) and for added aspirin treatment (\$12,710). For moderately aggressive treatment (blood pressure ≤ 85 mm Hg), the cost-effectiveness ratio escalated incrementally to \$86,360 and with intensive treatment to \$658,370 per year of life gained. Thus treatment to a target of 90 mm Hg and coadministering aspirin were considered highly cost effective, whereas treatments to lower the blood pressure further to 85 mm Hg were marginally cost effective; intensive blood pressure lowering down to 80 mm Hg was not cost effective.

The Hypertension Optimal Treatment (HOT) study showed that an aggressive antihypertensive treatment regimen led to impressive reductions in blood pressure and successfully reduced the cardiovascular adverse event rate.¹ The addition of aspirin to the antihyperten-

sive therapy provided additional protection in this study. From a societal perspective, the question arises: How cost effective is intensive treatment of hypertension? The costs of intensive antihypertensive therapy, the costs of adding aspirin to an antihypertensive regimen, and the comparisons of costs

and benefits were analyzed by Donald S. Shepard, PhD, Research Professor, and Dominic Hodgkin, PhD, Senior Research Associate, The Heller School, Brandeis University, Waltham, Massachusetts.

Cost-benefit and cost-effectiveness analysis are two types of economic analyses used to evaluate health interventions.²³ In cost-benefit analysis, both sides of the equation are expressed in monetary terms. Thus, for example, the benefit of improved health, is given a monetary value based on earnings or the value people place on improved health. Cost-effectiveness analysis is more widely used in the healthcare sector. In this type of analysis, all costs are quantified in monetary terms, but the benefits are expressed in effectiveness terms. Thus quality-adjusted life years (QALYs) or disability-adjusted life years (DALYs) are frequently used outcome measures that represent years of life weighted in some way for the effects of treatment and disease.

Figure 1. Annual Cost of Each Drug, by Dose

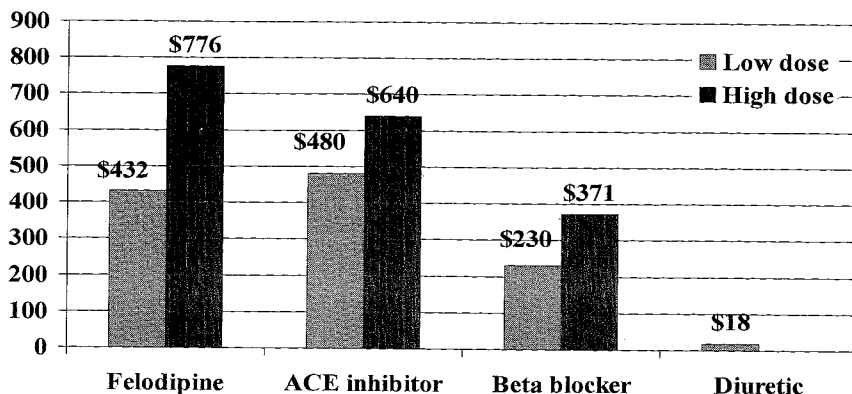
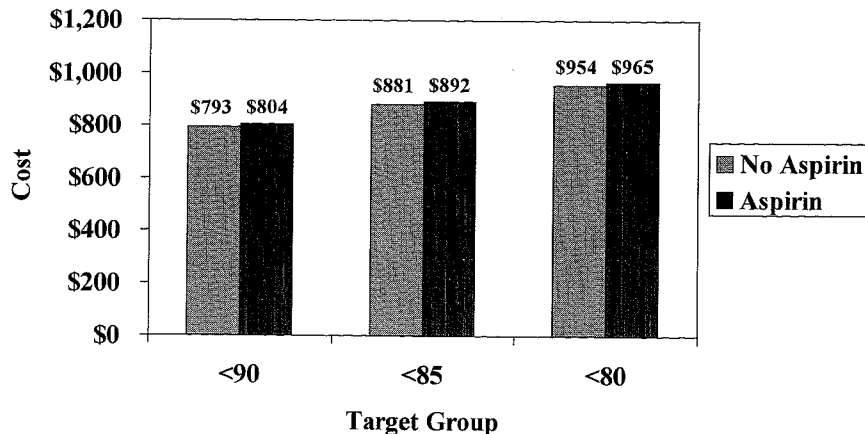


Figure 2. Annual Drug Cost by Blood Pressure



Estimation of Intervention Costs for the HOT Study

The first step in the analysis was to determine the annual cost for low and high doses for each of the drugs being used in the study. The average wholesale price was used as the baseline, with a 15% mark-up to reflect the retail price. Felodipine was the first-line drug, with an annual cost of \$432 for a low dose. Because more than one drug was available for the β -blocker and angiotensin-converting enzyme (ACE) inhibitor classes, which were used at step 2, an average annual cost for each of these drug classes was calculated from the annual cost for individual drugs. Steps 3 and 4 consisted of a doubling of the doses of felodipine and

ACE inhibitor or β -blocker, respectively. However, because of the more economical pricing structure for larger doses, the cost is less than twice as high. Figure 1 shows the annual costs for the high and low doses of the different drug classes.

Determination of Costs for Each Level of Blood Pressure Control

Given the study design, it is not enough to know the annual cost of each drug; one has to know how many patients were getting each combination of drugs. In the HOT study, hypertensive patients were randomized to three target blood pressure groups: ≤ 90 mm Hg, ≤ 85 mm Hg, and ≤ 80 mm Hg, and a five-step treatment regimen was instituted to facilitate achievement of goal-based blood pressure. Published data provide the number of patients at each of five titration steps by blood pressure group⁴ and we assumed that within each step, the distribution of patients by pharmacologic treatment was similar to the overall distribution at the end of the trial.¹ This made it possible to estimate the annual cost for patients at each step of treatment and by blood pressure target group. Thus, the annual costs increased from \$432 for patients who were still at step 1 to \$1390 for patients at step 5, the major incremental increases occurring at steps 2 and 3 when the ACE inhibitor or β -blocker was added and the dose of felodipine was doubled, respectively. The distribution of costs by blood pressure target group is shown in Figure 2. The costs for a patient in the most aggressively managed group (target blood pressure ≤ 80 mm Hg) were higher because more patients in this group were at steps 3, 4, or 5. The overall cost of managing hypertension should also include the costs of office visits and laboratory work, which from earlier work⁵ were estimated at \$400 annually. Thus annual overall costs range from approximately \$1200 for less aggressive treatment to approximately \$1400 for intensive treatment.

Cost Effectiveness of Alternative Regimens

To do a cost-effectiveness analysis, the health effects have to be converted into a single unit that is relevant and that can be related to other studies in the literature. The only outcome from the HOT study that was significantly correlated with the blood pressure target was the myocardial infarction (MI) risk per 1000 patient-years, which was 3.6, 2.7, and 2.6 for target groups ≤ 90 mm Hg, ≤ 85 mm Hg, and ≤ 80 mm Hg, respectively. On the basis of a fatality rate of 12.2 % (derived from earlier clinical trial data)⁶ for elderly patients with MI, the fatal MI risk per 1000 was calculated to be 0.4, 0.3, and 0.3 for the three blood pressure target groups, respectively (Table 1).

The next step was to convert the fatality risk into years of life lost. What Drs. Shepard and Hodgkin used in their analysis was a variant on that, namely DALYs, in which years of life are discounted for being in the future just as money in the future is discounted. For each 65-year-old person, whose death is averted, the undiscounted gain is 19 years, which computes to 9 DALYs per person. This translates into a large gain of 280

Table 1. Effects of Lower Blood Pressure

Health Effects	Diastolic Blood Pressure Target		
	≤ 90	≤ 85	≤ 80
MI risk/1000	3.6	2.7	2.6
Incremental MI/1000	n/a	0.9	0.1
Case fatality rate (%)	12.2	12.2	12.2
Fatal MI/1000	0.4	0.3	0.3
DALYs/fatality	9.16	9.16	9.16
DALYs per 1000	4.0	3.0	2.9
Cum DALYs/1000	280.0	281.0	281.1
Incr DALYs/1000	280.0	1.0	0.1

cumulative DALYs per 1000 patient-years for lowering the blood pressure from a baseline of 110 mm Hg to 90 mm Hg (this figure, approximating the patient's uncontrolled pressure, was based on the previous modeling work of Weinstein et al).⁵ Beyond that,

further lowering to 85 and 80 mm Hg provides a gain of only 1 DALY per 1000 patient-years. A similar calculation for the benefits of aspirin yields an incremental gain of 0.9 DALYs per 1000 patient-years with aspirin treatment.

The cost effectiveness (ie, dollars per life year gained) of the various interventions is presented in Figure 3. Going from no blood pressure control (eg, 110 mm Hg diastolic) to a target of 90 mm Hg in the elderly (age 60) is very cost effective, as Weinstein et al⁵ found with similar calculations, with a cost per DALY of about \$4000. Adding aspirin is very inexpensive at approximately \$13,000 per DALY. However, the cost increases rapidly to \$86,000 per DALY with moderately aggressive blood pressure control and then to nearly \$650,000 per DALY with the most aggressive regimen.

Another way to view cost effectiveness is: How does the economy value a year of life? If the per capita US gross national product is considered to be \$20,000, then that is a measure of the output gained by buying a year of life. In those terms, lowering blood pressure to 90 mm Hg (at a cost of \$4262 per DALY) and treating with aspirin (at a cost of \$12,710) are favorable interventions. "We could see this as a pretty good bargain, or a good way of buying a year of life," said Dr. Shepard. Lowering the blood pressure from 90 to 85 is a bit expensive but still arguable, he said. However with a further reduction to 80 mm Hg, the gains are rather small, the cost per unit of gain is very high and is about

Figure 3. Cost Per Discounted Life Year Gained (\$)

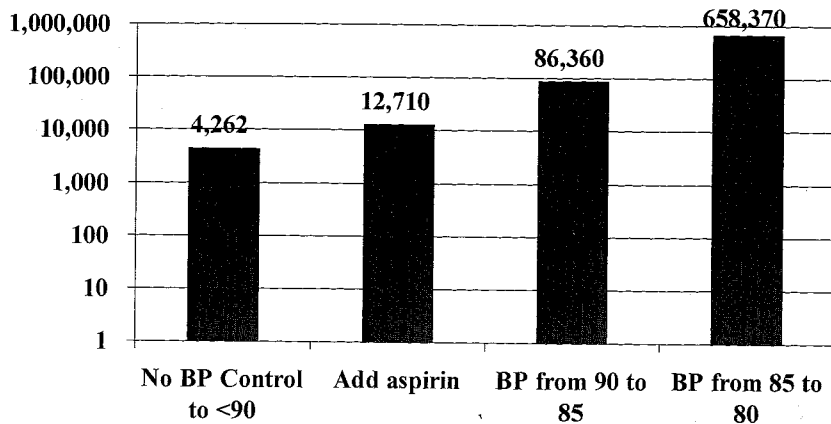
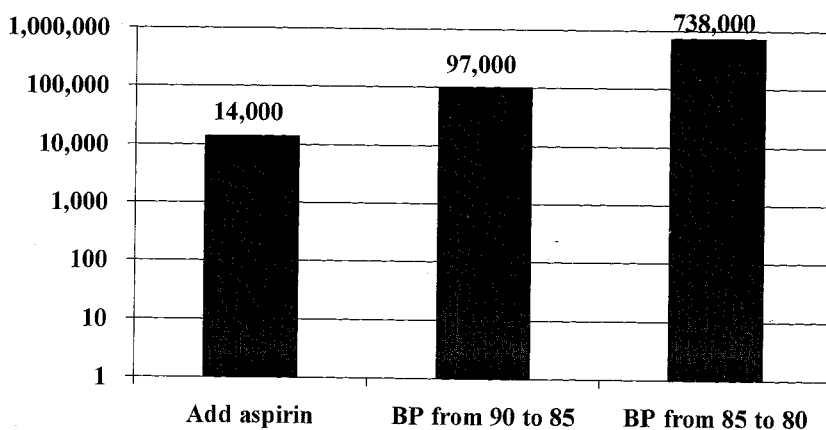


Figure 4. Cost Per Myocardial Infarction Averted (\$)



two orders of magnitude more than would be valued by the economy.

Finally, expressing the cost effectiveness in terms of averting one MI (Figure 4), the costs of antihypertension treatment plus aspirin to a blood pressure level of ≤ 90 mm were \$14,000; for blood pressure reduction from 90 mm to 85 mm, the cost was \$97,000; and further reduction to 80 mm Hg was achieved at a cost of \$738,000. With the most aggressive treatment, the cost would probably not be offset with savings in cardiovascular events.

... DISCUSSION HIGHLIGHTS ...

Dr. Wilson: You have 90, 85, and 80 mm Hg as the threshold blood pressure levels that you set on the graphs, but the actual levels achieved were 85, 83, and 81 mm Hg. So would it be better to use those levels on your graphs? My fear would be that people seeing this would assume that reducing the pressure from 90 mm Hg to 85 mm Hg is not beneficial when in fact, the pressure was actually reduced to 83 mm Hg. So 85 mm Hg is a beneficial target if viewed that way. Do you know the percentage of patients in each group who actually achieved the target blood pressure?

Dr. Messerli: You are, of course, correct. The differences in diastolic blood pressure between the three groups were much smaller than anticipated. This is the major reason that statistical power was lost. Nevertheless, the initial intent was to titrate the patients to achieve a difference of 5 mm Hg in diastolic pressure between the three groups.

Dr. Wilson: If they actually did a subgroup analysis, it would be interesting to see if there was greater improvement in those who did achieve the target blood pressure versus those who didn't.

Dr. Messerli: They did an analysis of quality of life and side effects, and it turned out that those who had the lowest blood pressures did best in terms of quality of life and side effects. It was totally the opposite of what one would expect.

Dr. Jacobs: Even if you relabel based on blood pressure achieved, doesn't your analysis depend on the treatment content of the individual groups? If you look at it in terms of the blood pressure lowering, how does that help you understand the cost since the cost is defined by the arm that the patient is in?

Dr. Brunton: The effects on blood pressure should not really be considered because the final outcome was given in relation to the target group.

Dr. Jacobs: So, one cannot determine what the cost effectiveness was of achieving the target blood pressure based on your data.

Dr. Shepard: That's correct. Data from the HOT study indicate the rate of MIs in patients with varying intensities of blood pressure control but not the rate that would have occurred with no blood pressure control whatsoever. Additional data from the literature are needed to determine the cost effectiveness of the least intensive level of blood pressure control: a diastolic blood pressure target of 90 mm Hg. The analysis by Dr. Hodgkin and me relied on data from the Framingham Study for this purpose. On the other hand, to compare a more stringent target (eg, 85 mm Hg) with a less stringent target (eg, 90 mm Hg), we could use internal data from the HOT Study, as outcome data were available for both of these target levels.

Dr. Wilson: You kept your nondrug costs stable between the three groups. We analyzed the effect of the number of modifications made to therapy on the number of visits made per year,

and there actually was a linear relationship. As the number of modifications of therapy increased, the number of visits per year as well as other nonmedical costs increased. Thus, achieving a lower target is going to require more modifications of therapy, and therefore costs wouldn't be stable between the three groups. There would therefore be another incremental cost in addition to that for drugs, and this would make more vigorous control even less cost effective.

Dr. Wagner: The interesting thing about these kinds of data are the differences between a patient's or a physician's perspective and a population's perspective. The individual looks at this as a bimodal decision—"I'm either going to die or not die; I'm either going to have a heart attack or not have a heart attack." It's not done on a risk-analysis basis, with calculation of DALYs or QALYs, and that's where we run into trouble in terms of applying this kind of evaluation. We don't think in the same terms as the data comes out.

Dr. Wilson: Dr. Messerli, do you know what the minimum diastolic pressure had to be for patients to be entered into the HOT study? The mean diastolic pressures in the three groups are pretty high relative to what I would have expected to see in a normal population of patients with hypertension.

Dr. Messerli: I believe it was over 95 mm Hg, but I could be wrong.

Dr. Hodgkin: One exclusion criterion was a blood pressure exceeding 115 mm Hg at entry into this study.

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