

Screening and Treatment for Subclinical Hypertensive Heart Disease in Emergency Department Patients With Uncontrolled Blood Pressure: A Cost-effectiveness Analysis

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ABSTRACT

Objectives: Poorly controlled hypertension (HTN) is extremely prevalent and, if left unchecked, subclinical hypertensive heart disease (SHHD) may ensue leading to conditions such as heart failure. To address this, we designed a multidisciplinary program to detect and treat SHHD in a high-risk, predominantly African American community. The primary objective of this study was to determine the cost-effectiveness of our program.

Methods: Study costs associated with identifying and treating patients with SHHD were calculated and a sensitivity analysis was performed comparing the effect of four parameters on cost estimates. These included prevalence of disease, effectiveness of treatment (regression of SHHD, reversal of left ventricular hypertrophy [LVH], or blood pressure [BP] control as separate measures), echocardiogram costs, and participant time/travel costs. The parent study for this analysis was a single-center, randomized controlled trial comparing cardiac effects of standard and intense (<120/80 mm Hg) BP goals at 1 year in patients with uncontrolled HTN and SHHD. A total of 149 patients (94% African American) were enrolled, 133 (89%) had SHHD, 123 (93%) of whom were randomized, with 88 (72%) completing the study. Patients were clinically evaluated and medically managed over the course of 1 year with repeated echocardiograms. Costs of these interventions were analyzed and, following standard practices, a cost per quality-adjusted life-year (QALY) less than \$50,000 was defined as cost-effective.

Results: Total costs estimates for the program ranged from \$117,044 to \$119,319. Cost per QALY was dependent on SHHD prevalence and the measure of effectiveness but not input costs. Cost-effectiveness (cost

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per QALY less than \$50,000) was achieved when SHHD prevalence exceeded 11.1% for regression of SHHD, 4.7% for reversal of LVH, and 2.9% for achievement of BP control.

Conclusions: In this cohort of predominantly African American patients with uncontrolled HTN, SHHD prevalence was high and screening with treatment was cost-effective across a range of assumptions. These data suggest that multidisciplinary programs such as this can be a cost-effective mechanism to mitigate the cardiovascular consequences of HTN in emergency department patients with uncontrolled BP.

Poorly controlled hypertension (HTN) is extremely prevalent in the United States,^{1–6} with a disproportionately high disease burden existing among African Americans, putting them at greater risk for poor cardiovascular outcomes such as stroke, myocardial infarction, chronic kidney disease, and heart failure (HF).^{1,7–11} Recommendations for therapy are well defined by the International Society of Hypertension in Blacks (ISHIB)¹² and in the recent Joint National Committee reports on HTN.^{13,14} However, due to factors that are difficult to overcome (therapeutic inertia, poor adherence to therapy, socioeconomic barriers, and patient understanding of disease state), achieving blood pressure (BP) control remains a challenge.^{1,13,15–21}

For patients with chronic but uncontrolled HTN, cardiac remodeling is a near-universal process that is associated with increased cardiovascular risk as it progresses. Despite this, underlying heart disease (HD) is typically not detected (or even screened for) until advanced remodeling is present and symptoms manifest,^{9,11,22–24} leaving clinicians with fewer options to prevent adverse events. Early identification of subclinical hypertensive heart disease (SHHD) and appropriate control of BP have become important steps in secondary cardiovascular disease prevention (especially for HF).^{11,25–28} Although some perceive that screening of asymptomatic patients provides no long-term benefit to morbidity,^{28–31} compelling arguments have been made for the utility of screening activities in communities that are predominately urban, African American and where limitations to healthcare access prompts heavy reliance on the emergency department (ED) for primary care.^{11,32–35} Increasing prevalence of the target condition is often tied to cost-effectiveness of such approaches and, in the case of SHHD, has direct implications for intensification of antihypertensive therapy.³⁶

The development of preventable secondary complications of SHHD leads to substantial increases in morbidity, mortality, and health care costs.³⁷ Multiple studies have demonstrated that uncontrolled HTN is a significant risk factor for the progression of SHHD and the onset of chronic HF and other clinically overt

conditions.^{1,7–11} Given the disproportionate burden of hypertensive heart disease in urban, African American populations, the primary objective of this study was to assess the cost-effectiveness of a multidisciplinary screening program designed to identify and treat SHHD among ED patients with elevated BP.

METHODS

Study Design and Setting

This cost-effectiveness analysis was an a priori aim included as part of a grant funded prospective, randomized controlled clinical trial (NCT00689819) designed to compare the effects of two BP targets (control, BP < 140/90 mm Hg [$<130/80$ mm Hg if diabetes or chronic kidney disease was present], and intervention, which had a singular target of $<120/80$ mm Hg) on reverse remodeling for patients with SHHD. Details of the study design, including SHHD determination and regression, have been previously published.³⁸ A convenience sample of patients who presented to a single-center ED located in Detroit, Michigan, where the population is 83% African American was enrolled between November 2008 and April 2010. Enrolled patients were evaluated at 3-month intervals over the course of 1 year in a single HTN clinic. Care was delivered by a multidisciplinary team including an ED physician, a HTN specialist experienced with HTN in our patient population, a physician's assistant (PA), a nurse practitioner (NP), research assistants, and clinic office staff. All care-related expenses, including transportation, telephone reminders, medications, and tests, were provided free of charge to all the participants. The institutional review board approved this study and all subjects provided written informed consent.

Selection of Participants

Study participants were recruited from a tertiary, academic medical center's ED, which treats over 90,000 patients each year. Over a 17-month period, individuals 35 years of age and older who presented with an initial BP $> 140/90$ mm Hg were identified using the

facility's electronic medical record (FirstNet by Cerner Corp.). For inclusion, patients were required to have a repeat BP > 140/90 mm Hg and have normal exertional tolerance (defined as class 1 on Goldman Specific Activity Scale). Those with acute illness requiring hospitalization, history of previously diagnosed coronary artery disease or HF, and presenting symptoms (i.e. dyspnea, chest pain) potentially attributable to hypertensive heart disease and those being actively followed and/or treated by primary care physician were excluded.^{11,38,39} Patients who met these criteria were brought back for a follow-up screening echocardiogram in our outpatient HTN clinic.

In total, 160 individuals met initial inclusion criteria, 149 of whom returned for a subsequent screening echocardiogram. All echocardiograms were performed and detailed history obtained for screened participants within 1 week. All participants with SHHD, defined by presence of left ventricular (LV) hypertrophy (LV mass ≥ 48 g/m^{2.7} in males or ≥ 45 g/m^{2.7} in females), LV systolic dysfunction (ejection fraction < 50%), or diastolic dysfunction (combination of parameters based on validated criteria of LV stiffness and relaxation) were randomized into either control or intensive therapy arms.¹¹

Study Procedures

Randomized participants were seen at baseline (initial visit) and 3-, 6-, 9-, and 12-month intervals. A standard BP measurement protocol was utilized. A trained research assistant, using appropriately sized oscillometric brachial cuff, performed three BP measurements with the patient in a seating position and their arms resting comfortably at heart level. The average reading of the three measurements was used to determine the BP reading recorded for that clinic visit. A multidisciplinary group of PAs and NPs then titrated antihypertensive therapy as needed, according to study group assignment. During each clinic visit, participants were educated about the importance of medication adherence and all received telephone reminders for pending follow-up appointments. Additionally, to help ensure compliance, all medication costs were paid for using study funds. Echocardiograms, all interpreted by a single board-certified cardiologist blinded to patient information and study group, were repeated at the 12-month visit. SHHD regression was the absence of left ventricular hypertrophy (LVH) and systolic or diastolic dysfunction on repeat imaging. Because LVH is such an important consequence of HTN and contributor to

important outcomes such as HF development, we also evaluated reversal of LVH (i.e., LV mass below threshold cut-points) as a separate outcome measure.

Cost Analysis

Total costs of the program (Table 1) were calculated by adding the cost of medications (based on purchase price from our outpatient pharmacy), laboratory tests (based on hospital research pricing), clinic activities (based on proportional space and personnel costs), echocardiograms (based on echocardiographic technician time), and participant time and travel. Time and travel costs were obtained through a survey and mean values of respondents were used to estimate a base case value of \$22.72 \pm \$14.36 per person. When data were missing, values for time and travel costs were imputed three different ways, separated by participants who did and did not complete the study: as zero (i.e., assumption of no cost), as the cohort median, and as the cohort mean. Based on this, low, median, and high total costs were estimated.

To evaluate cost-effectiveness, costs per quality-adjusted life-year (QALY) were calculated. This approach is widely accepted and QALYs have long been used to guide healthcare resource allocation.⁴⁰ A threshold cost of \$50,000 per QALY is the traditional benchmark for determining the value of care. Therefore, values at or below this were adopted in our study as the measure of cost-effectiveness.⁴¹⁻⁴³ The cost per QALY was modeled by the following mathematical equation, where 0.87 and 0.71 are used as standard utility values⁴⁴ assigned to patients for whom chronic

Table 1
Total Costs of Program With Imputed Values for Missing Values of Time and Travel Costs

Item	Completed Study Group (n = 88)	Drop-out Group (n = 45)	Total
Medications			\$43,778
Laboratory tests	\$5,408	\$3,749	\$9,158
Echocardiogram			\$29,517
Clinic Time			\$32,380
Zero	\$736	\$0	\$736
Median	\$1,448	\$891	\$2,339
Mean	\$1,476	\$1,157	\$2,633
Travel			
Zero	\$1,159	\$317	\$1,476
Median	\$1,159	\$581	\$1,740
Mean	\$1,159	\$695	\$1,854
Total			
Low	\$7,303	\$4,066	\$117,044
Median	\$8,015	\$5,221	\$118,912
High	\$8,044	\$5,600	\$119,319

HF (the most likely adverse consequence of untreated SHHD) would or would not be prevented by treatment, respectively:

the effect of disease prevalence, echocardiogram costs, and time/travel costs on cost per QALY using a base case that included the prevalence of SHHD in our

$$\frac{\text{Cost}}{\text{QALY}} = \frac{\text{Total cost}}{\left(\frac{\text{QALY}}{\text{year}} \text{ if effective} \times \text{expected life span} \times \text{probability of effectiveness} \right) + \left(\frac{\text{QALY}}{\text{year}} \text{ if not effective} \times \text{expected life span} \times \text{probability of not being effective} \right)}$$

$$= \frac{\text{Total cost}}{(0.87 \times 20(\% \text{ effective})) + (0.71 \times 20(1 - \% \text{ effective}))}$$

We based the probability of treatment effectiveness on preventing HF using three measures: regression of SHHD, reversal of LVH, and achievement of BP control. For purposes of this analysis, achievement of BP control was based on study randomization group targets rather than a singular BP goal. We varied the probability of successful outcome for each of these at 100, 50, and 25% for the low, median, and high end of the calculated program cost (Table 2) and then calculated the cost per case prevented, cost per QALY where HF would have been prevented and cost per QALY where HF would have developed. The variance levels for probabilities were selected to impart large, medium, and small impacts on the outcomes of interest.

Sensitivity analyses were then performed for each of our three treatment effectiveness measures, comparing

population, the proportion achieving the desired treatment effect for each measure, and a projected treatment effectiveness of 100% for SHHD and LVH regression and 50% for BP control. Medicare reimbursement rates were used to calculate adjusted total costs as influenced by changing echocardiogram costs, based on CPT code 93306 using national average global payments for 2013 and 2015, along with proposed future rates (Table 3).⁴⁵ Tornado plots were constructed, representing the impact of these predefined parameters on the overall cost per QALY.

RESULTS

Of the 149 subjects enrolled, 133 (89.3%) had SHHD, 123 (control n = 65, intervention n = 58)

Table 2
Program Cost Estimates Based on Projected Disease Probability of Outcome

Measure of Treatment Effectiveness	Program Cost Estimates and Projected Treatment Effectiveness								
	Low, \$117,044			Median, \$118,912			High, \$119,319		
	100%	50%	25%	100%	50%	25%	100%	50%	25%
Cost per case prevented									
BP control	\$3,259	\$6,519	\$13,038	\$3,320	\$6,639	\$13,279	\$3,333	\$6,666	\$13,331
SHHD regression	\$10,104	\$20,209	\$40,418	\$10,291	\$20,582	\$41,165	\$10,332	\$20,664	\$41,238
LVH regression	\$5,052	\$10,104	\$23,409	\$5,146	\$10,291	\$23,782	\$5,166	\$10,332	\$23,864
Cost per QALY-HF prevented									
BP control	\$3,747	\$7,493	\$14,986	\$3,816	\$7,632	\$15,236	\$3,831	\$7,662	\$15,324
SHHD regression	\$11,614	\$23,228	\$46,457	\$11,829	\$23,658	\$47,316	\$11,876	\$23,751	\$47,503
LVH regression	\$5,807	\$11,614	\$26,907	\$5,914	\$11,829	\$27,336	\$5,938	\$11,876	\$27,430
Cost per QALY-HF developed									
BP control	\$4,591	\$9,182	\$18,363	\$4,676	\$9,351	\$18,703	\$4,694	\$9,388	\$18,777
SHHD regression	\$14,232	\$28,463	\$56,926	\$14,495	\$28,989	\$57,978	\$14,552	\$29,104	\$58,208
LVH regression	\$7,116	\$14,232	\$32,970	\$7,249	\$14,495	\$33,496	\$7,276	\$14,552	\$33,611

Cost per case prevented, cost per QALY where HF would have been prevented, and cost per QALY where HF would have developed were estimated using various probability of successful outcomes (100%, 50%, 25%) for the low, median, and high end of the calculated program cost.
BP = blood pressure; HF = heart failure; LVH = left ventricular hypertrophy; QALY = quality-adjusted life-year..

Table 3
Adjusted Total Costs Based on Variable Echocardiogram Costs

Echocardiogram Cost (Variable)	Adjusted Costs		
	At \$268 (proposed)	At \$173 (2013)	At \$229 (2015)
Cost for 149 screened + 88 completed therapy	\$63,516	\$41,001	\$54,273
Difference*	\$33,999	\$11,484	\$24,756
Adjusted totals			
Low	\$151,043	\$128,528	\$141,800
Median	\$152,911	\$130,396	\$143,668
High	\$153,318	\$130,803	\$144,075

*Difference = the added cost arising from using Medicare pricing as the input variable for echocardiogram cost rather than the research cost noted in Table 1, which was based primarily on echocardiographic technician time.

were randomized, and 88 (control $n = 45$, intervention $n = 43$) completed the entire study protocol. The study population was mostly female (66%), and African-American (95%), with a mean (\pm SD) age of 49.2 (\pm 8.3) years. The majority of patients (82.9%) had been previously diagnosed with HTN, only 28 (23%) of whom were on prescribed medication at baseline and had carried the diagnosis, on average, treated for 8.8 (SD \pm 8.6) years. At initial screening in the ED, patients had a mean (\pm SD) systolic BP of 182.5 (\pm 23.3) mm Hg and a mean (\pm SD) diastolic BP of 104.8 (\pm 12.3) mm Hg. At randomization following the screening echocardiogram, mean (\pm SD) systolic BP was 151.2 (\pm 24.1) mm Hg and mean (\pm SD) diastolic BP was 97.2 (\pm 15.8) mm Hg. Of the 88 patients that completed therapy, 10 (11%) achieved SHHD regression, 20 (23%) experienced reversal of LVH, and 31 (35%) achieved BP control according to study specified goals.

Total estimated costs of the program (Table 1) ranged from \$117,044 to \$119,319. As shown in Table 2, the program was cost-effective (cost per QALY $<$ \$50,000) under all circumstances, except when the projected effectiveness of SHHD regression was $<$ 25% (Table 3). That is to say, our approach would be cost-effective if the patient has a 25% or greater probability of preventing HF with any of our treatment effectiveness measures (SHHD regression, LVH regression, or BP control), across a range of cost assumptions. The cost per QALY for all three treatment effectiveness measures was consistently below the \$50,000 mark when assessing cost per case

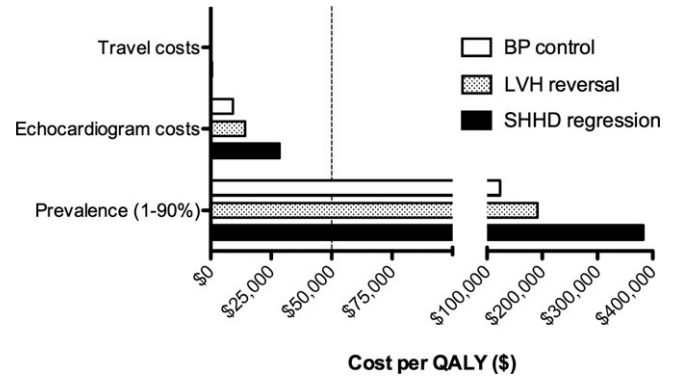


Figure 1. Cost per QALY for people achieving BP control, reversal of LVH, and regression of SHHD. Only prevalence decreases the cost per QALY below the \$50K mark, which occurs at a prevalence of $>$ 2.9% for BP control, $>$ 4.7% for LVH regression, and $>$ 11.1% for SHHD regression. Note: Travel cost data are hidden by the Y-axis. BP = blood pressure; LVH = left ventricular hypertrophy; QALY = quality-adjusted life-year; SHHD = subclinical hypertensive heart disease.

prevented and cost per case where HF would have been prevented.

Sensitivity analyses demonstrated that for each of the three measurable treatment effects, only prevalence of SHHD moves the overall cost per QALY above the \$50,000 mark. Specifically, overall cost per QALY exceeded \$50,000 only at prevalence rates below 11.1% for SHHD regression, 4.7% for LVH reversal, and 2.9% for BP control (Figure 1).

DISCUSSION

In this study of hypertensive ED patients, we found that a multidisciplinary program focused on detection and treatment of SHHD was cost-effective across a range of cost assumptions. This is important because SHHD is a meaningful point where intervention can prevent potential life-threatening conditions.¹²⁻¹⁴ However, for many with HTN, especially African Americans in underserved communities, heart disease will not be detected until advanced stages, limiting options for secondary or even tertiary prevention.^{9,11,22-24} While no one would suggest that ED physicians assume primary responsibility for the management of SHHD, in settings similar to ours where SHHD is likely to be prevalent, it is reasonable for the ED to play an active role in screening and referral. This process could include no more than BP readings and referral for a follow-up echocardiogram. Blood pressure readings are a routine measure taken as part of an ED patient visit and do not add to the total cost of care. Although echocardiograms are relatively expensive, not readily available in many EDs, and require

(as of now) a dedicated technician and physician to read the results, they are superior to electrocardiograms when assessing for SHHD.⁴⁶

Whether actual prevalence of disease in other communities will approach what we found in this study (89.3%) is unclear. Levy et al.¹¹ previously showed that within a similar population—underserved African American, hypertensive ED patients—the prevalence of underlying SHHD is close to 90%. The prevalence of SHHD in other patient populations with HTN has not been well described; however, existing studies suggest it broadly ranges between 0.9 and 50%.^{10,11,47–51} Given that the highest calculated prevalence rate when cost per QALY exceeds the \$50,000 mark in our data is 11%, it is likely that a similar program would remain cost-effective in the majority of other locations. It is important to note that for many disease states, the cost-effectiveness of screening is mutually exclusive from that of treatment. However, for the purposes of our study, no distinction was made between the cost of screening and the cost of treatment, as we sought to evaluate a program aimed at reducing the consequences of SHHD on an at-risk population—a process that involves both detection and ongoing management. To that end, we chose prevention of HF as the desired endpoint of treatment and constructed our cost-effectiveness models using HF as the outcome of interest. We did so because, of all the consequences associated with SHHD, HF is the most tightly linked overall and one that disproportionately affects African Americans.⁵² Moreover, prevention of HF through more comprehensive upstream screening for SHHD and intervention when present has become an area of increasing emphasis.⁵³

Based on our sensitivity analysis, the true cost-effectiveness of our approach to diagnosis and treatment of SHHD likely sits between \$20,000 and \$30,000 per year—a figure that is similar to recently published data by Moise et al.⁴³ that found more intensive BP control to be cost-effective at <\$50,000 per QALY for management of HTN, particularly in patients with cardiovascular disease, chronic kidney disease, and a 10-year cardiovascular disease risk > 15%. In a recent perspective piece, Neumann et al.⁴¹ argue that the \$50,000 per QALY measure may indeed be too low. As part of their analysis, they examined cost-effectiveness thresholds referenced by authors from 1990 to 2012. A majority of the studies reference \$50,000 as the most widely used benchmark,^{43,54} with \$100,000 being the second most popular value. Braithwaite et al.⁵⁵ further

suggest that a range between \$95,000 and \$264,000 per life-year saved should be considered when evaluating impact of care. In a study conducted by Shirowa et al.,⁵⁶ willingness to pay for one additional QALY was measured to be \$62,000. Although the usefulness of the \$50,000 benchmark has been questioned, and many other benchmarks have been proposed, the fact remains that no one measure is appropriate in all decision contexts.⁴¹ We chose to adopt the \$50,000 benchmark for our study because we thought it to be consistent with the economic reality of our study demographic. Using higher thresholds would only provide further evidence to support the cost-effectiveness of our approach, as there were few scenarios where sensitivity analysis exceeded the \$50,000 mark and none that were greater than \$62,000.

Problems with therapeutic inertia, poor adherence, socioeconomic challenges to self-care, and low disease-specific knowledge are known to affect HTN control.^{1,13,15–21} Accordingly, throughout the study, participants periodically filled out questionnaires aimed at accurately gauging, among other things, their time and travel costs. In analyzing responses, a majority indicated distance-to-travel to receive care as an important factor in their adherence and follow-up. As travel did not affect cost effectiveness in our study, paying for this and other potential barriers to follow-up for chronic HTN as part of a broad risk reduction program might be reasonable to consider.

LIMITATIONS

Several limitations to our study exist. This was a single-center trial with a limited number of subjects, over a relatively short time period, and this did not allow us to study cardiovascular outcomes over a longer period of time. The patient population was predominantly low-income and African American with poor access to primary medical care, making our results more difficult to apply across different demographic populations. However, this is a representative sample from a high-risk, underserved, and underrepresented population. As has been established previously, the prevalence of cardiovascular disease is exceedingly high within this demographic and SHHD is the only factor that determines the cost effectiveness of our treatment model, suggesting that our data are, at the least, applicable to similar high-risk populations. This study also had a high dropout rate in both control and intervention groups (28 and 24%, respectively) which was not unexpected

considering the study population and how these at-risk communities typically interact with the health system.

Another limitation is that the design of our mathematical model to determine QALY did not assign hazard ratios to measure regression versus nonregression of end-stage disease. We believe that this would have led to a more accurate assessment of HF progression. Additionally, the increased costs associated with developing HF—i.e., hospitalizations, interventions, loss of productivity, etc.—were not added to the equation except for in the adopted utility factors. It can be argued that by not including such data, the development of HF has little impact on the cost-effectiveness of our program. However, we believe that addressing specific outcomes is not essential in building a strong argument for intervention. Many different adverse consequences are expected as a result of uncontrolled HTN and utility measures adopted are the most productive way to represent the broad nature of possible outcomes. Finally, we assigned just one-life-year gained, which may be underrepresenting the actual benefits of disease regression. However, had we used a lengthier time measure, our results would have only been further validated.

Finally, this is a cost-effectiveness study, rather than one that measures (patient specific) willingness to pay for treatment. Such an investigation was beyond the scope of this study but may merit future research.

CONCLUSIONS

Our approach to screen for and treat subclinical hypertensive heart disease among urban ED patients with elevated blood pressure proved to be cost-effective across a range of cost- and treatment-effectiveness assumptions. The prevalence of subclinical hypertensive heart disease was particularly high in our predominantly African American cohort, many of whom utilize the ED for primary care, suggesting that multidisciplinary programs designed to prevent cardiovascular complications of hypertension could be beneficial in similar communities.

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