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Effectiveness and Cost-Effectiveness of Blood Pressure Screening in Adolescents in the United States

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Abstract

Objective—To compare the long-term effectiveness and cost-effectiveness of 3 approaches to managing elevated blood pressure (BP) in adolescents in the United States: no intervention, “screen-and-treat,” and population-wide strategies to lower the entire BP distribution.

Study design—We used a simulation model to combine several data sources to project the lifetime costs and cardiovascular outcomes for a cohort of 15-year-old U.S. adolescents under different BP approaches and conducted cost-effectiveness analysis. We obtained BP distributions from the National Health and Nutrition Examination Survey 1999–2004 and used childhood-to-adult longitudinal correlation analyses to simulate the tracking of BP. We then used the coronary heart disease policy model to estimate lifetime coronary heart disease events, costs, and quality-adjusted life years (QALY).

Results—Among screen-and-treat strategies, finding and treating the adolescents at highest risk (eg, left ventricular hypertrophy) was most cost-effective ($18 000/QALY [boys] and $47 000/ QALY [girls]). However, all screen-and-treat strategies were dominated by population-wide strategies such as salt reduction (cost-saving [boys] and $650/ QALY [girls]) and increasing physical education ($11 000/QALY [boys] and $35 000/QALY [girls]).

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Conclusions—Routine adolescents BP screening is moderately effective, but population-based BP interventions with broader reach could potentially be less costly and more effective for early cardiovascular disease prevention and should be implemented in parallel.

Hypertension affects one in 3 adult Americans and is a major risk factor for coronary heart disease (CHD), stroke, and end-stage renal disease.[1] Among US adolescents, blood pressure (BP) levels have risen substantially in recent decades, largely because of the obesity epidemic.[2] Although end-stage organ damage is rare in children, childhood BP is the strongest predictor of adult hypertension.[3,4] The evidence base is well established for the clinical value of diagnosing and treating adults with hypertension, either by medication or lifestyle change.[1,5] Whether such "screen-and-treat" approach is equally effective and cost-effective in adolescent hypertension is unknown.

Currently, annual BP screening is recommended for children 3 years of age and older by the American Academy of Pediatrics, the National Heart, Lung, and Blood Institute, the American Medical Association, and the American Heart Association. In contrast, the US Preventive Services Task Force concludes that evidence is insufficient to recommend for or against routine BP screening in children and adolescents. On the other hand, all guidelines endorsed a public health approach to lower the entire pediatric BP distribution, despite limited evidence on its potential long-term impact. Although a decades-long clinical trial would inform the comparative effectiveness of different childhood BP strategies, it is unlikely to occur because of its high cost and time frame. A modeling framework to integrate multiple pieces of clinical and epidemiologic evidence is therefore required to address the effectiveness and cost-effectiveness of adolescent BP screening. In this study, we combined data on BP measurement, tracking, and intervention effect and predicted the lifetime effectiveness on reducing CHD events and associated medical costs under various BP management approaches among US adolescents with the CHD Policy Model.

Methods

We evaluated 3 approaches: (1) no screening/intervention; (2) "screen-and-treat;" and (3) population-wide strategies to lower BP of all adolescents. Under the "screen-and-treat" approach, we examined routine screening for all 15-year-olds, as well as selectively screening only overweight adolescents. Once elevated BP is found, adolescents were treated by individual-based behavioral programs, such as exercise, low-salt diet, and, if overweight, weight reduction. We also evaluated a variation of the screening strategy: treating only those with the highest risk, that is, secondary hypertension or left ventricular hypertrophy (LVH). Finally, we evaluated two hypothetical public health strategies that aim to lower the entire BP distribution, albeit with smaller effect for each individual: policy actions to reduce dietary salt intake and increasing physical education (PE) classes in schools.

Two-Phased Model Structure (Figure 1; available at www.jpeds.com)

Phase 1: Age 15 to 35 Years—We simulated a cohort of 2 065 127 boys and 1 952 694 girls (2000 US census). We estimated 20-year (age 15 to 35) longitudinal tracking coefficients (1) from combined data of the 8- to 12-year East Boston Study of 337 children and the 16-year follow-up of 822 Framingham Offspring Study subjects (Table I; available

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at www.jpeds.com). We grouped the baseline 15-year-old cohort into 3 diastolic BP categories: <79, 79–83, and >83 mm Hg (cutoffs correspond to the 90th and 95th percentile for 15-year-olds of median height).[6] We used the tracking correlations, the BP distribution at age 15, and intervention effectiveness to predict BP distributions at age 35, the entry point to the CHD Policy Model (Appendix 1; available www.jpeds.com).

Phase 2: Age 35 Years to Death: CHD Policy Model—The CHD Policy Model is a Markov cohort model of CHD incidence, prevalence, death, and costs in the US population aged 35 years and older (Appendix 2; available at www.jpeds.com). The demographic-epidemiologic submodel predicts incidence of CHD and deaths from other causes, stratified by age, sex, and up to 6 additional categorized risk factors: diastolic blood pressure ([DBP] <80, 80–90, >90 mm Hg), smoking status, high-density lipoprotein (HDL) cholesterol (<40, 40–59, ≥60 mg/dL), low-density lipoprotein (LDL) cholesterol (<100, 100–129.9, ≥130 mg/dL), BMI (<25, 25–29, >30 kg/ m^2), and diabetes mellitus. The distributions of risk factor categories derive from the National Health and Nutrition Examination Survey (NHANES) 1999–2004. Each state and event has an annual cost and health-related quality-of-life adjustment.[7] All simulated cohorts follow an age-related trend in mean BP, hypertension treatment, and disease incidence based on US data.

BP Screening among US Adolescents

We estimated BP distributions (systolic or diastolic BP ≥95th percentile, 90th–95th percentile, or <90th percentile)[6] of U.S. adolescents 13–17 years of age (averaging age 15) from NHANES 1999–2004 (n = 3887).[8] We defined overweight as body mass index (BMI) at or above the age- and sex- specific 85th percentile on the basis of the growth standards of the Centers for Disease Control and Prevention.[9]

We assumed that BMI and BP measurements occur during routine well-child visit and incur no marginal cost, but two additional office visits are required to confirm a diagnosis of hypertension.[6] We assumed that 30% of children with high first-visit BP would consistently have hypertension throughout 3 visits.[10] In our base case, we assumed that 30% of adolescents with hypertension have LVH.[11] We assumed that most adolescents with elevated BP had essential hypertension, and 5% of them have secondary causes.[12] We estimated that diagnostic tests to establish causes and comorbidities cost $659 (Table II).[13]

Effectiveness and Costs of Individual-Based Behavioral Interventions

We used estimates from meta-analyses for the effectiveness of interventions on diastolic BP: weight reduction (−3.59 mm Hg),[14] exercise (−2.00 mm Hg),[15] and salt restriction (−1.29 mm Hg) (Table II).[16] In our base case analysis, we assumed that the effects of these interventions decline by 5% every year. This assumption was a conservative estimate on the basis of the reported maintenance of intervention effect among studies reviewed in the 3 meta-analyses.[14–16] We subsequently varied this assumption in the sensitivity analysis from 0% to 10%. We also estimated the average cost of a 12-month weight management program to be $941 and an exercise program similar to Project ACTIVE[17] to be $710 per participant. Dietary counseling programs focusing on salt reduction were assumed to involve 4 weekly hour-long sessions by nutritionists and cost $515.[18]

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Among the 5% of adolescents with secondary hypertension, we assumed that 10% of them have potentially curable conditions such as renal artery stenosis or aortic coarctation.[19] We assumed that treatment cost $30 000 per case,[20,21] and once diagnosed, these adolescents would be treated effectively and safely. For the remaining 90% of secondary hypertension cases, we assumed they would receive antihypertensive medications.[22]

Effectiveness and Costs of Population-Wide Interventions without Screening

Voluntary reduction in salt content by food manufacturers combined with a mass-media campaign could achieve a 15% population-wide reduction in salt intake,[23] approximately 27% of the effect size from salt-reduction trials. Proportionally, we assumed that population-wide salt-reduction campaigns would result in 27% of the BP-lowering effect of an individual-based intervention (ie, 0.27 × −1.29 mm Hg = −0.35 mm Hg) and cost $1.70/ person.[23] On the basis of the median salary of secondary school teachers,[18] adding two PE classes per week for 3 academic years would cost ~$183/ student.

Cost-Effectiveness Analysis

For the base case analysis, we calculated the average lifetime cost and health effects, including number of CHD events, life-years, and quality-adjusted life years (QALYs) of all screening and intervention strategies, as well as no screening or intervention. We adopted a societal perspective and discounted all future direct medical costs and health effects at 3% annually.[24] We calculated cost-effectiveness ratios for each strategy as costs per QALY gained compared with no screening/intervention, as well as incrementally compared with all other less costly alternatives.[24]

In a series of sensitivity analyses, we varied each parameter input for cost-effectiveness one at a time to reflect the impact of uncertainty on base case result. In a scenario analysis, we accounted for the potential non-BP cardiovascular benefits from weight reduction, that is, lower LDL cholesterol, higher HDL cholesterol, and lower diabetes risk.[25] Finally, we modified the Model to use systolic BP instead of diastolic BP to characterize BP-related cardiovascular risks and the effectiveness of childhood screening and treatment.

Results

With the recommended cut points,[6] the prevalence of elevated BP at one screening visit among NHANES adolescents was 26% for boys and 7.5% for girls. After two follow-up visits, we estimated that the prevalence of confirmed hypertension and prehypertension was, respectively, 3.9% and 22.1% in boys and 1.9% and 5.6% in girls. From East Boston Study and the Framingham Offspring Study, the estimated longitudinal tracking coefficients from age 15 to 35 were 0.30 for males and 0.37 for females, consistent with other reported values.[26]

Cost-Effectiveness of Strategies Compared with No Screening/Intervention

Compared with no screening/treatment, we estimated that routine screening and treating adolescents who have prehypertension or hypertension would increase life expectancy by 2.1 to 8.6 days among 15-year-old boys and by 0.5 to 1.8 days among girls (Table III). The

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average cost-effectiveness (compared with no screening/intervention) of routine BP screening followed by individual-based weight loss, exercise, or salt reduction interventions, ranging from $61 000 to $67 000 per QALY gained for boys and $116 000 to $135 000 per QALY gained for girls (Figure 2; available at www.jpeds.com). Selectively screening overweight adolescents (strategy 2g) was more cost-effective than routinely screening all adolescents ($54 000/QALY for boys and $103 000/QALY for girls; Table III). Conversely, routine BP screening followed by diagnosis and treatment only for adolescents with LVH or secondary hypertension (strategy 2f), a "high-risk only" approach, resulted in quite attractive average cost-effectiveness ratios: $18 000/QALY for boys and $47 000/QALY for girls.

As a comparison, hypothetically treating all adolescents without BP screening in fact results in lower screening costs but higher treatment and overall costs, as well as greater QALY gains than screen-and-treat strategies. For instance, forgoing BP screening and treating all overweight adolescents with weight-loss programs (strategy 3a) avoided ~649 000 BP screenings but treated ~525 000 more overweight teens. As a result, for the same BP treatment option, (eg, weight loss, the cost-effectiveness for treating all overweight adolescents without screening [3a–3c]) was more attractive than the corresponding screen-and-treat strategy (Table III). Finally, population-wide policy interventions (3f and 3g) appear extremely cost-effective. A population-wide salt-reduction campaign was cost-saving for boys and cost only ~$650/QALY for girls. Adding PE classes in high schools was valued at $8000 per QALY gained for boys and ~$29 000 per QALY gained for girls, relative to no screening or intervention.

Incremental Cost-Effectiveness Analyses

In a separate, incremental analysis, the cost-effectiveness of each strategy was evaluated by comparing its additional costs and its additional effectiveness relative to other less costly alternatives. Considering all strategies altogether, a population-wide salt reduction campaign (3g), increased PE classes (3f), and treating everyone with a structured exercise program (3d) dominated all screening strategies, meaning screen-and-treat approaches are more costly and less effective than their alternatives (Figure 3 and Table IV; available at www.jpeds.com). Increasing PE classes, a "passive" population-based approach to increasing physical activity among adolescents, was more attractive ($11 000/QALY for boys and $35 000/QALY for girls) than individual-based exercise programs for adolescents (~$55 000/QALY for boys and ~$120 000/QALY for girls).

When we only compared among screening strategies, routine screening followed by treating secondary hypertension and LVH (2f, the "high-risk only" screening strategy) was cost-effective ($18 000/QALY for boys and $47 000/QALY for girls). Compared with such strategy, routine screening followed by treating individuals with hypertension (2d) was not very cost-effective: $69 000/QALY for boys and $386 000/QALY for girls.

Sensitivity Analysis

The average cost-effectiveness ratio of routine screening and treatment (strategy 2d) was relatively stable across most parameter inputs. One exception was the assumed discount rate (Figure 4), for example, compared with no screening, the cost-effectiveness of strategy 2d

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varied from ~$8000 to $336 000 per QALY (base case: $62 000) for boys and from $16 000 to $602 000 (base case: $103 000) for girls when the discount rate varied from 0% to 7%. The rate of decline in treatment effect also substantially affects the cost per QALY estimates (eg, the cost-effectiveness ratio varied from ~$5000 to $349 000 for boys and from $20 000 to $334 000 for girls per QALY as the annual decline changed from 0% to 10%).

When we assumed that weight loss has benefit beyond BP-lowering but also improves cholesterol and diabetes risk, selectively screening and treating overweight adolescents became more cost-effective. The most attractive screen-and-treat strategy was 2g—selective screening of overweight adolescents and treating those found to have hypertension with weight loss programs (~$5000/QALY for boys, ~$7000/ QALY for girls, compared with no screening). The next most attractive strategy was 2e, routine screening followed by weight loss or salt reduction (~$65 000/QALY in boys and ~$77 000/QALY in girls). Routine screening followed by weight loss or exercise (2d) also had a reasonable incremental cost-effectiveness ratio relative 2e (~$87 000/QALY in boys and $117 000/QALY in girls). Despite these ancillary benefits of weight loss boosting the cost-effectiveness of screen-and-treat strategies, population-wide approaches to adolescent BP control still dominated all screening strategies in the incremental cost-effectiveness analysis. A salt reduction campaign remained the most attractive (cost saving in boys and ~$650/QALY in girls). Adding PE classes, however, was dominated by individual-based weight loss interventions for all overweight adolescents without BP screening ($13 000/ QALY for boys and $20 000/ QALY for girls).

When a systolic BP-based model is used, the cost-effectiveness ratio of routine BP screening and treating obese adolescents with weight loss and nonobese adolescents with salt reduction (strategy 2e) were $68 000/QALY in boys and $90 000/QALY in girls, compared with the base case results of $62 000/QALY in boys and $116 000/QALY in girls. All other screening strategies were still dominated by other alternatives in the incremental analysis. Population-wide salt reduction continued to be much more cost-effective ($6000–18 000/ QALY) than routine screening (incremental cost-effectiveness ratio of strategy 2e: $87 000/ QALY in boys and $166 000/QALY in girls).

Discussion

In this report, we used a modeling framework to demonstrate the effectiveness and cost tradeoffs between different approaches to early prevention of cardiovascular diseases through lowering BP in adolescence. We found that a routine screen-and-treat strategy could be effective in preventing future CHD burden but is not very cost-effective. Our analysis also suggests that a broad-reaching, policy-based intervention such as salt reduction or increasing PE classes could potentially be more cost-effective than most screen-and-treat strategies. This conclusion rests on the observation that a large number of future cases of CHD occur among youths with normal BP rather than those who have prehypertension or hypertension at age 15.[27] However, the study underlines the value of public health approaches to lowering cardiovascular risk in the pediatric population. Of similar reasoning, Cook et al[5] estimated that lowering diastolic BP by just 2 mm Hg among all persons 35 to 64 years of age could reduce stroke risk by 14% and CHD risk by 6%. More recently,

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Bibbins-Domingo et al[28] demonstrated that the cardiovascular benefits from reducing a modest 1 g/d of dietary salt at the population level could be comparable with use of medications to lower BP in adults with hypertension.

There are several explanations for the more stark contrast between the effectiveness of screen-and-treat and population approaches in adolescents than in adults, in whom hypertension treatment is much more cost-effective.[29] Only a small proportion of adolescents are eligible for pharmacotherapy; behavioral interventions tend to have low compliance and modest effects. As a result, the difference in treatment efficacy between individual-based BP-lowering programs and policy/ environmental approaches is narrower in childhood than in adulthood. Moreover, BP tracks imperfectly over long periods; many adolescents who are diagnosed with hypertension eventually have normal BP at older ages when BP better correlates with short-term cardiovascular risks. Effective treatment targeted at adults with hypertension is therefore more likely to result in immediate clinical benefits. Many adolescents with elevated BP who went through behavioral programs, however, would only accrue small benefit decades later, if at all.

A number of assumptions should be acknowledged which may make our cost-effectiveness analyses of adolescent BP screening unduly pessimistic. We assumed that the BP reduction resulted from behavioral changes earlier in life represent the same cardiovascular benefit as medically-treated hypertension later of the same magnitude. However, drug-treated hypertension in adults does not eliminate cardiovascular risks to the same extent as in patients with naturally-low BP.[30] In addition, atherosclerosis starts in youth and may be more amenable to BP-lowering interventions. It is therefore possible that a lower BP achieved by behavioral interventions in childhood is more beneficial than treating adults with hypertension.[31] Furthermore, we did not consider any synergy between BP interventions. For example, exercise improves the success of weight management, and weight loss also decreases BP sensitivity to salt.[32] On the other hand, several assumptions might have led to optimistic estimates for screen-and-treat approach. We did not include quality of life decrement consequent to screening or intervention. Although obtaining a BP causes minimal discomfort, the disutility of undergoing further evaluation and behavioral interventions could be substantial. We did not include the time costs for making follow-up visits and receiving behavioral treatments, likely making screening and individual-based interventions appear more cost-effective.

The results of our model-based study are further constrained by the assumptions made and the uncertainty with the parameter inputs. Variations on the cost and effectiveness of treatment options can certainly alter the cost-effectiveness estimates. We did not consider the potential differences by race-ethnicity; however, studies have shown little racial-ethnic differences in adolescences than in adulthood.[10] Despite these limitations, from a population standpoint, the rank-ordering of strategies appear stable across a wide range of parameter values, and we believe the base case analyses provide reasonable order-of-magnitude valuation of cost-effectiveness.

Because overweight and obesity are strongly linked with multiple cardiovascular risk factors, we were not surprised that our sensitivity analysis that included non-BP beneficial

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effects of weight loss showed selective screening of overweight adolescents to be more cost-effective than routine screening. Nevertheless, when we considered all approaches, population-wide strategies such as salt reduction and a weight loss program remained both less costly and more effective.

Preventing hypertension and its cardiovascular sequelae therefore should start in youth, especially in the face of the childhood obesity epidemic. Although BP screening and treatment of youths with hypertension are recommended as part of routine pediatric care, our results suggest that a screen-and-treat approach alone to childhood BP may not deliver the best “bang for the buck” at the population level. Policy and environmental interventions that broadly affect BP level of all youths may be more effective and more cost-effective; it is thus of high priority to ensure the implementation of these strategies in parallel to any expansion of clinical services to screen and treat children and adolescents with elevated BP.

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Glossary

BP	Blood pressure
CHD	Coronary heart disease
DBP	Diastolic blood pressure
HDL	High-density lipoprotein
LDL	Low-density lipoprotein
LVH	Left ventricular hypertrophy
NHANES	National Health and Nutrition Examination Survey
QALY	Quality-adjusted life years

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Appendix 1

Calculations of Positive Predictive Values with Longitudinal Tracking Coefficients

We used the positive predictive value (PPV) to calculate the probability that children with observed mean diastolic blood pressure levels (y_{i0}) at or above the 95th percentile (k) after three screens will have an observed mean diastolic blood pressure (y_{it}) greater than the cutoff point z in young adulthood. The positive predictive value can be expressed as follows:

$$PPV=\Pr(\overline{y}_{it}>z|\overline{y}_{i0}>k)=\frac{\int_{z}^{\infty}\left[1-\Phi\left(\frac{k-C}{d}\right)\right]\frac{1}{\sqrt{2\pi(\sigma_{Pt}^2+\sigma_{Wt}^2)}}\exp\left[\frac{-(x-\mu_{Pt})^2}{2(\sigma_{Pt}^2+\sigma_{Wt}^2)}\right]dx}{1-\Phi\left(\frac{k-\mu_{P02}}{\sqrt{\sigma_{Po}^2+\sigma_{Wo}^2}}\right)}$$

where $C=\mu_{P0}+\rho_{0t}\left(\frac{\sigma_{P0}\bullet\sigma_{Pt}}{\sigma_{Pt}^2+\sigma_{Wt}^2}\right)(x-\mu_{Pt})$ and $d^2=(1-\rho_{0t}^2)\sigma_{P0}^2+\sigma_{w0}^2$ and where $\mu_{pj}(x)$ is the expected mean of the population at time j, ρ_{0t} is the longitudinal tracking correlation from child-hood to young adulthood correlated for within-person variability, σ_{Pj}^2 is the between-person variance and σ_{Wj}^2 is the within-person variance at time j, and Φ is the cumulative normal distribution, this computational form for positive predictive value is mathematically equivalent to a more familiar expression: positive predictive value=(sensitivity × prevalence)/[(sensitivity × prevalence)+(1 − specificity) × (1 − prevalence)].

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Appendix 2

The CHD Policy Model is a computer-simulated, state-transition (Markov cohort) model of CHD incidence, prevalence, mortality, and costs among persons older than 35 years in the U.S. population.[1] In the version we used for this analysis, we apportioned persons age 35 to 85 years in the U.S. population with no history of CHD into 32 400 risk cells, de-fined by 6 modifiable risk factors: diastolic blood pressure (<80, 80 to 89.9, or ≥90 mm Hg), LDL cholesterol level (<2.6, 2.6 to 3.3, or ≥3.4 mmol/L [<100, 100 to 129.9, or ≥130 mg/dL]), HDL cholesterol level (<1.0, 1.0 to 1.5, or ≥1.6 mmol/L [<40, 40 to 59.9, or ≥60 mg/dL]), smoking status (active smoker, nonsmoker with exposure to environmental tobacco smoke, or nonsmoker without environmental exposure), diabetes mellitus (yes or no), and statin use (yes or no), as well as by sex and 10-year age range. We apportioned persons with prevalent CHD into 1300 cells according to their age, sex, and history of myocardial infarction, cardiac arrest, angina, or revascularization.

We determined CHD incidence and non-CHD deaths in persons with no previous CHD by logistic risk functions on the basis of Framingham longitudinal data.[2] Transitions in the disease history component of the model were based on age range–specific event and case fatality rates estimated from national data and literature-based relative risks for events among disease history subgroups (such as previous myocardial infarction vs. none). Non-CHD mortality rates among persons with CHD reflected the relative risk of non-CHD death for this sample in the Framingham data. In the absence of evidence of a trend, we assumed all of these rates remained constant. Absolute numbers of events vary with temporal changes in the population, the age range distribution of the population, and in response to user-defined interventions.

All population distributions, risk factor levels, coefficients, event rates, case-fatality rates, costs, and quality-of-life adjustments can be modified for forecasting simulations. We ran the model on Fortran 95 (Lahey Computer Systems, Incline Village, Nevada).

CHD Prevalence

We estimated the background prevalence of CHD in 2000 from the National Health Interview Survey.[3] We estimated the background prevalence of previous revascularization procedures from revascularizations before 2000 and estimated survival after revascularization from the National Hospital Discharge Survey (NHDS)[4] and other studies.[5,6]

CHD Deaths

We obtained data on CHD deaths from the 2000 Vital Statistics Mortality Data.[7] We estimated CHD deaths on the basis of International Classification of Diseases, 10th revision, codes I20 to I25, I46, and 2/3 of I49, I50, and I51.[8,9] We considered other deaths to be non-CHD deaths.

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Cardiac Arrest (Sudden Death) with Resuscitation

The number of persons who survive from cardiac arrest to hospital discharge was estimated from the NHDS[4] for 1990 to 1999. Because this number is small in any given year, we averaged the national estimates over the 10-year period.

We estimated prehospital cardiac arrest fatalities on the basis of Vital Statistics Mortality Data for selected causes by place of death.[10] For International Classification of Diseases, 10th revision, codes I20 to I25, we assumed all emergency department deaths and those dead on arrival to be deaths from cardiac arrest. We considered all nursing home deaths to be chronic CHD deaths. We estimated that resuscitation was attempted for all in-residence and “other place” deaths on the basis of reported resuscitation rates for witnessed[11] or unwitnessed[12] cardiac arrest.

Proportion of Cardiac Arrests with No History of CHD

The CHD history is harder to ascertain for patients with cardiac arrest than for those with myocardial infarction because no national registry exists, the numbers are smaller, and fewer studies are available. We estimated the age range–specific proportions of cardiac arrest with and without a history of CHD by a least-squares fit to data from multiple sources.[13,14]

Myocardial Infarction

We estimated myocardial infarction target incidence as the average annual number of discharges coded as 410 in the NHDS 2000 data set. We eliminated records of myocardial infarction in which hospital stay was fewer than 3 days and no acute revascularization was done in the same hospitalization as probable “rule out myocardial infarction” cases. We reduced remaining counts by the double count fraction reported by Westfall and McGloin[15] and applied an additional 3% deduction for miscoding, as reported by Petersen et al.[16]

Myocardial Infarction Case-Fatality Rates

We obtained mean number of myocardial infarction deaths per adjusted total myocardial infarction from the NHDS, 1996 to 2000, for the older age ranges (65 to 84 years) and used the National Registry of Myocardial Infarction[17] for in-hospital case-fatality rates for the younger age ranges (35 to 44 years). Studies of young patients with myocardial infarction estimate an in-hospital mortality rate of 1% to 6%, compared with a rate of 8% to 22% for older patients.[18]

We estimated in-hospital and 30-day case-fatality rates from hospital discharge records from the State of California Office of Statewide Health Planning and Development for the year 2000.[19] The in-hospital case-fatality rate was based on unique person records (duplicate entries eliminated by matching social security numbers). We omitted a small number of records that did not have social security numbers. The overall rate ratio of 30-day case-fatality rate to in-hospital case-fatality rate was 1.28953 (12.07/9.36). We used this ratio to adjust national inhospital case-fatality rates to 30-day mortality rates.

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On the basis of the study by Rieves et al,[20] we incorporated a mortality odds ratio of 1.6 for patients with previous myocardial infarction and 1.17 for patients with previous angina. Subset case-fatality rates were calculated to reflect these odds ratios and preserve the overall estimated case-fatality rate for myocardial infarction.

Revascularization Rates

We estimated the number of percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG) procedures from the NHDS for 2000. We adjusted the revascularization rate to reflect a repeated revascularization rate for PCI and for CABG in the first year. We estimated a trend in the ratio of PCI to CABG for 2000 to 2004. We assumed that PCI would be included as part of the treatment for myocardial infarction in the same proportion observed in the NHDS data set for 2000, with emergency CABG complicating 2% of these procedures. We included reductions in mortality and reinfarction rates for patients treated with PCI.[21,22]

Risk Functions for Incident CHD and Non-CHD Death

We determined incident CHD cases (myocardial infarction, cardiac arrest, or angina) and non-CHD deaths in each risk factor cell for the at-risk U.S. population by using risk functions (r) that incorporated age- and sex-specific parameters (α) and risk factor–specific β-coefficients (β_k; k = 1, 2, 3, … , 6), which are constant over the time span of a simulation, and cell-specific risk factor means (m_k; k = 1, 2, 3, … , 6), which are altered by user-defined intervention:

We determined β-coefficients for non-CHD death from the same examination sets of the Framingham cohort and offspring data that we used for the CHD β-coefficients, but with diastolic blood pressure, smoking, and diabetes as the only statistically significant covariates in the logistic regression analysis.

We estimated overall incidence of CHD and non-CHD death by age range and sex for 2000 by adjusting the Framingham incidence estimates for 1986 to take into account the trends in risk factor means from 1986 to 2000. We estimated the corresponding values of the intercepts by iterative fitting of the risk function to the overall incidence. We estimated incidence of cardiac arrest without previous CHD by using the proportion of cardiac arrest without previous CHD in Olmsted County[13] and incidence of myocardial infarction by using the proportion of myocardial infarction without previous CHD in several published studies that analyzed data from the National Registry of Myocardial Infarction 2,[23] the Cardiovascular Cooperative Project,[24] and the Worcester Heart Attack study.[17,25]

We assumed all risks and rates to be constant over time, in the absence of evidence of a trend. We incorporated trends as they became apparent, such as that for the use of revascularization between 2000 and the present, but did not project them into the future. The CHD and non-CHD death risk functions are applied to every state in every year of a simulation to accommodate the competing risk for these 2 outcomes naturally over time.

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Incident CHD Event Allocation

We assumed that risk factors would affect the incidence of myocardial infarction, cardiac arrest, and angina in proportion to overall incidence, except we assumed smoking had a higher relative risk for infarction and cardiac arrest[26] and a proportionately lower coefficient for angina. We assumed that environmental tobacco exposure carried a relative risk of 1.26 for myocardial infarction and cardiac arrest, compared with nonexposed nonsmokers,[27] but did not influence angina.

Risk Factor Prevalence and Correlations Between Risk Factors

We estimated the prevalence of each risk factor level and correlations among risk factors (and thus the apportionment of the U.S. population without CHD into the 3240 risk cells) from National Health and Nutrition Examination Study (NHANES), 1999 to 2004.[28]

Transitions between Risk Factor Levels

We included transfers from 1 risk factor level to another to preserve the NHANES proportions of the population with each risk factor level. For example, the proportion of men 35 to 44 years of age in the lowest DBP category (<80 mm Hg) is 0.628. For men 45 to 54 years of age, the proportion is 0.558. The shift toward higher DBP levels is associated with increasing BP in middle age. In higher age ranges, this trend reverses, so that by age 75 to 84 years, the proportion is 0.874. The change in the upper age ranges is probably caused by a more complex array of factors, such as people with higher risk being more likely to die.

Costs and Quality-of-Life Adjustments

We estimated total health care costs from the perspective of the health care system by using national data.[29] We estimated the CHD cost component by using California data,[19] deflated by using cost-to-charge ratios[30] and the ratio of the U.S. national average costs to the California average[31] and then inflated to 2006 dollars by using the Bureau of Labor Statistics Consumer Price Index for Medical Care Costs.[32] We based health-related quality-of-life weights on observational data[33] and discounted costs and QALYs at a rate of 3% per year.

Quality Control and Validation

The CHD Policy Model was calibrated to reproduce national data on risk factor distributions, total CHD deaths, acute myocardial infarction, witnessed sudden cardiac death and revascularization procedures in the base year. Validation of projections into the future is an ongoing effort in which the model's results under a broad range of scenarios are compared with data from studies, clinical trials, and surveys, obtained from public sources or by personal communication. Validation required reasonable agreement in outcomes when the conditions that produced the data were incorporated. For example, simulations of persons in the US population age 45 to 64 years that imposed the before and after LDL cholesterol and HDL cholesterol levels recorded in the WOSCOPS (West of Scotland Coronary Prevention Study)[34] resulted in similar results for the cumulative percentage of the

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cohort to have died of CHD or have had a first myocardial infarction, as well as for the ratio of events in participants who were and were not treated with statins.

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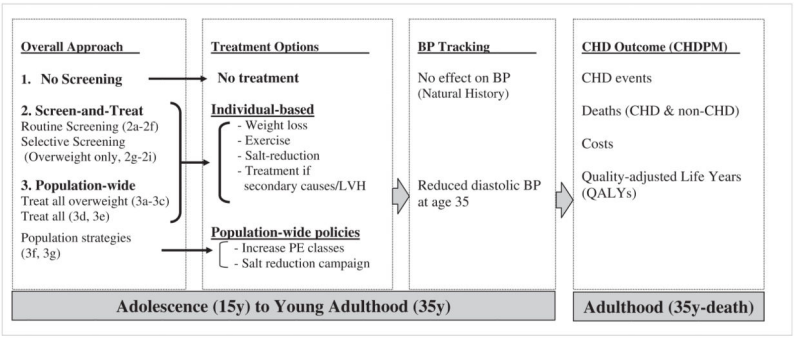

BP: Blood Pressure; PE: Physical Education; CHD: Coronary Heart Disease; CHDPM: Coronary Heart Disease Policy Model

Figure 1.
Schematic diagram of the two-phased BP screening model.

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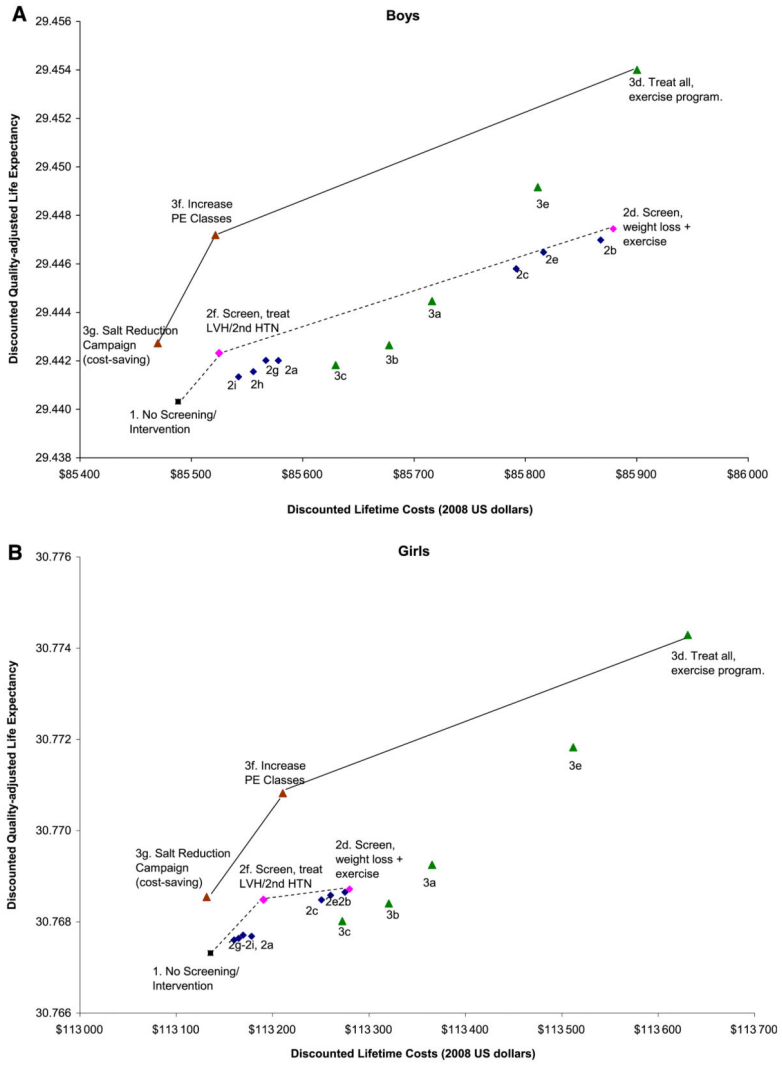
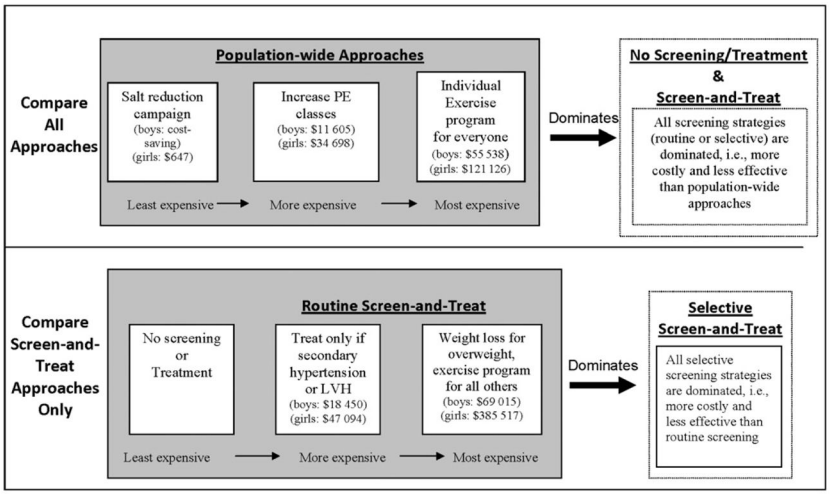


Figure 2.

Average discounted lifetime costs (in 2008 dollars) and quality-adjusted life expectancy (years) for 15-year-old adolescents under different BP screening and intervention strategies, compared with no screening/intervention. **A,** Boys; **B,** Girls. Connecting lines are cost-effectiveness efficiency frontiers linking strategies that are not dominated by their alternatives. *Solid lines* correspond to the incremental cost-effectiveness analysis that compares all 3 types of strategies (*Squares* = no screening/ intervention, *circles* = screen-and-treat, and *triangles* = population-wide strategies). *Dotted lines* correspond to the incremental cost-effectiveness analysis that compares screening strategies only.



PE: Physical education; LVH: Left ventricular hypertrophy. Shaded boxes represent non-dominated strategies under the incremental cost-effectiveness analyses; Units are dollars per quality-adjusted life year saved (discounted by 3% annually)

Figure 3.

Results of incremental comparisons of adolescent blood pressure control strategies. Summary of two separate incremental cost-effectiveness analyses.

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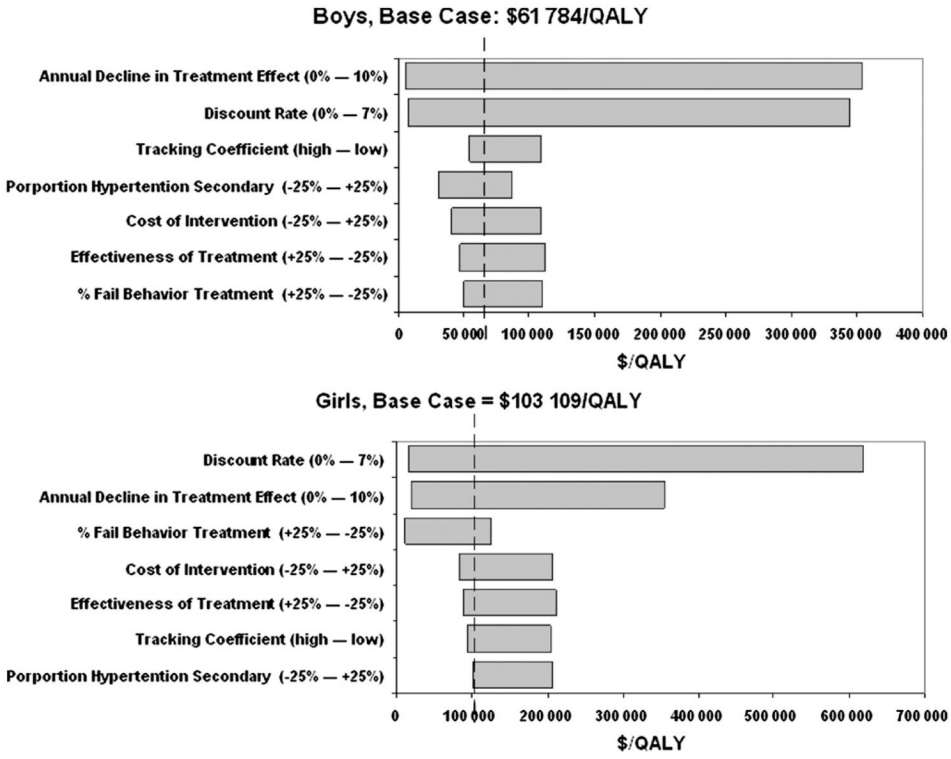

Figure 4.

Sensitivity analyses (Tornado diagram): showing the degree to which uncertainty in individual variables affects the average cost-effectiveness ratio of routine BP screening followed by weight loss (if overweight) or exercise (if normal weight), compared with no screening/treatment. Ranges for annual decline in treatment effect and for discount rate are absolute percents. Other ranges are ± changes relative to base case.

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Table I

Effect of longitudinal tracking coefficient values on the distribution of projected diastolic blood pressures at age 35 years, based on diastolic blood pressure at age 15 years

			DBP distribution at age 35 years		
Sex	**DBP at age 15 years***	**Longitudinal tracking correlation†**	**<80 mm Hg**	**80–90 mm Hg**	**>90 mm Hg**
Male	>83 mm Hg	0	66.7	24.4	8.8
		0.19 (lower bound)	54.8	30.5	14.7
		0.30 (midpoint)	47.4	33.7	18.9
		0.42 (upper bound)	39	36.7	24.2
		1	1.4	28.5	70.1
	79–83 mm Hg	0	66.7	24.4	8.8
		0.19 (lower bound)	57.7	29.2	13
		0.30 (midpoint)	52.2	32	15.8
		0.42 (upper bound)	45.8	35.2	19
		1	5.5	51	43.5
	<79 mm Hg	0	66.7	24.4	8.8
		0.19 (lower bound)	67.2	24.1	8.5
		0.30 (midpoint)	68.1	23.7	8.1
		0.42 (upper bound)	69.4	23.1	7.4
		1	72.7	22.2	5.0
Female	>83 mm Hg	0	83	14	3
		0.32 (lower bound)	69	23.8	7.3
		0.37 (midpoint)	66.4	25.5	8.1
		0.43 (upper bound)	63.1	27.6	9.2
		1	15.9	60.9	23.2
	79–83 mm Hg	0	83	14	3
		0.32 (lower bound)	73.9	20.6	5.4
		0.37 (midpoint)	72.4	21.8	5.8
		0.43 (upper bound)	70.5	23.3	6.2
		1	41.5	54.1	4.4
	<79 mm Hg	0	83	14	3

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Sex	DBP at age 15 years*	Longitudinal tracking correlation†	DBP distribution at age 35 years		
			<80 mm Hg	80–90 mm Hg	>90 mm Hg
		0.32 (lower bound)	84.2	13.2	2.7
		0.37 (midpoint)	85.7	12.1	2.2
		0.43 (upper bound)	87.6	10.7	1.7
		1	93.7	5.9	0.4

*Based on the 90th and the 95th percentile for 15-year-old boys and girls of median height from the Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents.[1]

†Longitudinal tracking correlations of diastolic blood pressure corrected for within-person variance.

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Table II

Baseline values for model variables, key assumptions, and sources

Parameter	Base Case	Source
Epidemiology of hypertension and screening		
Prevalence of elevated BP at one screen	26% (M), 7.5% (F)	NHANES
%Confirm hypertension given elevated BP at first screen	30.24%	Sorof et al[10]
Prevalence of secondary hypertension	5%	Published data
Proportion of secondary hypertension curable	10%	Prevalence of renal artery stenosis or coarctation of aorta[19,32]
% Hypertensive adolescents with left ventricular hypertrophy	30%	Published studies[11]
Discount rate	3%	
Costs		
Preventive visit to pediatrician's office	$95	U.S. Average based on AAP estimates
Diagnostic workup for established hypertension for secondary causes or end-organ damage such as left ventricular hypertrophy	$659	Medicare payment rate for phlebotomy, electrolytes, urea nitrogen, and creatinine, lipid profile, complete blood count, urinalysis, fasting glucose, echocardiography, and renal ultrasound.
Treatment of secondary hypertension	$30 000	Published estimates for coarctation of the aorta and renal artery stenosis[20,21]
Individual-based weight reduction	$941	Average between two intervention arms in Goldfield et al[33]
Individual-based exercise program	$710	Average between two intervention arms in Sevick et al[17]
Individual-based dietary counseling on salt reduction	$515	4 weekly sessions with dietician[18]
Pharmacotherapy	$334/year	Published estimates
Increase PE classes in high schools	$183/student	Adding 2 classes per week for 3 years (two 18-week semesters per school year), assuming median wage for high school teachers[18] and average class size of 40.
Policy to promote salt reduction in food & media-based education	$1.70/person	Upper bound of published estimates in upper middle-income countries to achieve a 15% reduction in salt intake.[23]
Effectiveness of BP Treatments		
Weight reduction program, effect on DBP	−3.57 mm Hg	Published meta-analysis[14]
Effect of exercise program on DBP	−2.00 mm Hg	Published meta-analysis[15]
Effect of salt reduction program on DBP	−1.29 mm Hg	Published meta-analysis[16]
Effect of pharmaceutical treatment on DBP	−8.60 mm Hg	Silverstein et al[22]
% fail individual-based program to achieve BP goal	50%	Expert opinion
Annual decline in treatment effectiveness	5%	Assumption
Effect of increasing PE classes on DBP	−1.00 mm Hg	Assumed half of exercise program
Effect of population-based salt reduction on DBP	−0.35 mm Hg	27% of dietician-based salt reduction programs[23]

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Table III

Costs and effects of blood pressure control strategies for adolescents in 2000, relative to no screening or intervention

Strategy	Life years gained	ΔCost* (×$1000)	Δ QALYs*	Cost per QALY†
Boys				
1. No Screening or intervention (status quo comparator)				
2. Screening BP, followed by interventions for adolescents with elevated BP Universal screening, if high BP:				
2a. Weight loss program if obese	11 324	$193 642	3130	$61 874
2b. Exercise program	44 495	$814 462	12 319	$66 113
2c. Salt reduction program	36 603	$652 267	10 134	$64 364
2d. Weight loss program if obese, exercise program otherwise	47 590	$839 880	13 177	$63 739
2e. Weight loss program if obese, salt reduction otherwise	41 116	$706 153	11 387	$62 016
2f. Pharmacologic or surgical treatment if secondary hypertension/LVH	14 914	$76 116	4125	$18 450
Selective screening: screen overweight adolescents only, if high BP:				
2g. Weight loss program	11 329	$170 633	3142	$54 309
2h. Exercise program	8238	$145 216	2284	$63 573
2i. Salt reduction program	6773	$116 770	1880	$62 121
3. Population-wide approaches to lower entire BP distribution: Individual-based behavioral programs without screening (active)				
3a. Weight loss program for all overweight adolescents	27 658	$490 272	7657	$64 027
3b. Exercise program for all overweight adolescents	15 514	$402 214	4298	$93 586
3c. Salt reduction program for all overweight adolescents	10 013	$299 330	2774	$107 921
3d. Exercise program for all adolescents	91 435	$915 306	25 303	$36 174
3e. Salt reduction program for all adolescents Policy or environmental strategies (passive)	59 077	$708 388	16 350	$43 325
3f. Increasing PE classes	45 861	$101 434	12 694	$7991
3g. Salt reduction campaign	16 041	($26 431)	4442	($5950)
Girls				
1. No Screening or intervention (status quo comparator)				
2. Screening BP, followed by interventions for adolescents with elevated BP Universal screening, if high BP:				
2a. Weight loss program if obese	2424	$85 828	633	$135 654
2b. Exercise program	8669	$281 807	2290	$123 078
2c. Salt reduction program	7582	$233 038	2002	$116 409
2d. Weight loss program if obese, exercise program otherwise	9102	$291 687	2405	$121 285
2e. Weight loss program if obese, salt reduction otherwise	8225	$252 309	2174	$116 066
2f. Pharmacologic or surgical treatment if secondary hypertension/LVH Selective screening: screen overweight adolescents only, if high BP:	8683	$107 508	2283	$47 094
2g. Weight loss program	2549	$69 143	673	$102 692
2h. Exercise program	2096	$59 433	555	$107 088
2i. Salt reduction program	1866	$50 033	494	$101 317

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Strategy	Life years gained	ΔCost* (×$1000)	Δ QALYs*	Cost per QALY†
3. Population-wide approaches to lower entire BP distribution: Individual-based behavioral programs without screening (active)				
3a. Weight loss program for all overweight adolescents	12 578	$463 147	3317	$139 611
3b. Exercise program for all overweight adolescents	7069	$369 290	1865	$198 063
3c. Salt reduction program for all overweight adolescents	4548	$272 467	1202	$226 728
3d. Exercise program for all adolescents	45 438	$1 017 770	11 971	$85 018
3e. Salt reduction program for all adolescents Policy or environmental strategies (passive)	29 380	$767 923	7743	$99 172
3f. Increasing PE classes	22 830	$172 116	6017	$28 604
3g. Salt reduction campaign	7999	$1364	2110	$647

*Discounted at 3% per year.

†Cost-effectiveness ratio compared to no screening or intervention, also referred to as the average cost-effectiveness ratios.

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Table IV

Incremental cost-effectiveness analyses

	Boys		Girls	
Base Case Results				
1. Compare all strategies	Non-dominated Strategies	ICER	Non-dominated Strategies	ICER
	3g. Salt reduction campaign	Cost saving	3g. Salt reduction campaign	—
	3f. Increasing PE classes	$ 11 605	3f. Increasing PE classes	$ 34 698
	3d. Exercise program for all	$ 55 538	3d. Exercise program for all	$ 121 126
Dominated*	1, 2a–2i, 3a–3c, 3e–3g		1, 2a–2i, 3a–3c, 3e–3g	
2. Compare only screening strategies	Non-dominated Strategies	ICER	Non-dominated Strategies	ICER
	1. No Screening or intervention	—	1. No Screening or intervention	
	2f. Screen & treat only secondary hypertension/LVH	$ 18 450	2f. Screen & treat only secondary hypertension/LVH	$ 47 094
	2d. Screen all+ weight loss if overweight, exercise otherwise	$ 69 015	2d. Screen all+ weight loss if overweight, exercise otherwise	$ 385 517
Dominated*	2a–2c, 2e, 2g–2i		2a–2c, 2e, 2g–2i	
Alternative Scenario: Assuming Weight Loss Also Lowers LDL and Diabetes and Increases HDL				
1. Compare all strategies	Non-dominated Strategies	ICER	Non-dominated Strategies	ICER
	3g. Salt reduction campaign	Cost saving	1. No Screening or intervention	—
	3a. Weight loss program for all	$ 13 648	3g. Salt reduction campaign	$ 647
	3d. Exercise program for all	$ 201 239	3a. Weight loss program for all	$ 19 715
Dominated*	1, 2a–2i, 3b–3c, 3e–3f		1, 2a–2i, 3a–3c, 3e–3g	
2. Compare only screening strategies	Non-dominated Strategies	ICER	Non-dominated Strategies	ICER
	1. No Screening or intervention	—	1. No Screening or intervention	—
	2g. Screen overweight+ weight loss	$ 5181	2g. Screen overweight+ weight loss	$ 7116
	2e. Screen all+ weight loss if overweight, salt reduction otherwise	$ 65 076	2e. Screen all+ weight loss if overweight, salt reduction otherwise	$ 76 893
	2d. Screen all+ weight loss if overweight, exercise otherwise	$ 86 699	2d. Screen all+ weight loss if overweight, exercise otherwise	$ 117 297
Dominated*	2a–2c, 2e, 2g–2i		2a–2c, 2e, 2g–2i	

*A strategy of screening or intervention costs more but was less effective than its alternatives and was therefore dominated.