Prevention and Treatment of Hypertension Study (PATHS): Effects of an Alcohol Treatment Program on Blood Pressure

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Objectives: To determine whether blood pressure is reduced for at least 6 months with an intervention to lower alcohol intake in moderate to heavy drinkers with above optimal to slightly elevated diastolic blood pressure, and whether reduction of alcohol intake can be maintained for 2 years.

Design: A randomized controlled trial.

Methods: Six hundred forty-one outpatient veterans with an average intake of 3 or more alcoholic drinks per day in the 6 months before entry into the study and with diastolic blood pressure 80 to 99 mm Hg were randomly assigned to a cognitive-behavioral alcohol reduction intervention program or a control observation group for 15 to 24 months. The goal of the intervention was the lower of 2 or fewer drinks daily or a 50% reduction in intake. A subgroup with hypertension was defined as having a diastolic blood pressure of 90 to 99 mm Hg, or 80 to 99 mm Hg if recently taking medication for hypertension.

Results: Reduction in average weekly self-reported alcohol intake was significantly greater ($P<.001$) at every assessment from 3 to 24 months in the intervention group vs the control group: levels declined from 432 g/wk at baseline by 202 g/wk in the intervention group and from 445 g/wk by 78 g/wk in the control group in the first 6 months, with similar reductions after 24 months. The intervention group had a 1.2/0.7–mm Hg greater reduction in blood pressure than the control group (for each, $P = .17$ and $P = .18$) for the 6-month primary end point; for the hypertensive stratum the difference was 0.9/0.7 mm Hg (for each, $P = .58$ and $P = .44$).

Conclusions: The 1.3 drinks per day average difference between changes in self-reported alcohol intake observed in this trial produced only small nonsignificant effects on blood pressure. The results from the Prevention and Treatment of Hypertension Study (PATHS) do not provide strong support for reducing alcohol consumption in nondependent moderate drinkers as a sole method for the prevention or treatment of hypertension.

Arch Intern Med. 1998;158:1197-1207

**Alcohol consumption has been shown in epidemiological studies** to have one of the strongest associations with blood pressure (BP) among the known potentially modifiable risk factors for hypertension. This direct relationship is most consistent above 2 drinks per day (a standard drink is defined as approximately 14 g of ethanol and is contained in a 12-oz glass of beer, a 5-oz glass of table wine, or a 1.5-oz glass of distilled spirits) average intake and generally persists even when controlling for confounding variables such as age, body mass, and sodium and potassium excretion. Prospective observational studies have indicated that reduction in alcohol consumption is associated with reduction in BP, and inpatient studies of alcoholics have reported that detoxification often results in a decrease in BP.

Randomized controlled trials provide a high level of evidence for the efficacy of an intervention. However, as recently reviewed, only 10 randomized studies have been conducted to examine the effect of a reduction in alcohol intake on BP. These relatively few studies usually included few subjects, were also generally of short duration, and were not designed as effectiveness trials. Therefore, the National Heart, Lung, and Blood Institute, Bethesda, Md, and the National Institute on Alcohol Abuse and Alcoholism, Rockville, Md, along with the Veterans Affairs Cooperative

The affiliations of the authors appear in the Acknowledgment section at the end of the article. Members of the PATHS Group are listed on page 1206.
PARTICIPANTS AND METHODS

The methods and other aspects of the design and organizational structure of PATHS have been described in detail. In brief, this was a randomized, parallel group trial primarily comparing the effects on BP of an intervention to decrease alcohol intake vs nonintervention in nondependent moderate to heavy drinkers (≥21 drinks per week or ≥294 g/wk) with above optimal to slightly hypertensive levels of DBP. Ambulatory male and female veterans aged 21 to 79 years, who on a brief self-administered pre-screening questionnaire reported consuming an average of at least 10 drinks weekly during the previous 6 months, were invited for the first screening visit. After consent was obtained, use of any antihypertensive medications was discontinued at least 2 weeks before beginning the screening phase. Evaluations during the 3-visit screening phase included medical history; BP, weight, and heart rate determinations; physical examination; local and central laboratory studies, including biochemical markers of alcohol intake, urine drug screen, and urinary sodium, potassium, and magnesium excretion; psychosocial and health habits assessment; dietary and physical activity questionnaires; assessment of alcohol intake and alcohol dependence; and an echocardiogram. All but the medical history and physical examination and screen for alcohol dependence were repeated at specified intervals during follow-up.

The Alcohol Dependence Scale was self-administered at the first screening visit to exclude candidates who evidenced manifestations of alcohol dependence, since it was considered unethical to withhold some form of intervention from dependent drinkers. The primary alcohol eligibility criterion was based on a structured interview instrument (Lifetime Drinking History) administered at the second screening visit. To be eligible a participant must have reported consumption of an average of at least 21 drinks per week in the most recent 6 months.

Blood pressure was measured in the right arm with a random-zero mercury sphygmomanometer using a BP cuff appropriate for arm circumference. Systolic BP (SBP) was phase 1 and DBP was phase 5 of the Korotkoff sounds. The “visit blood pressure” was the average of 2 measurements taken 30 seconds apart with the bell of the stethoscope after the participant sat quietly for 3 minutes in a back-supported chair.

Blood pressure eligibility was 75 to 109 mm Hg diastolic and lower than 200 mm Hg systolic at the first screening visit and for the average of all the readings from the first 2 screening visits, and 80 to 99 mm Hg diastolic and 179 mm Hg systolic or lower for the average of the 6 readings from all 3 screening visits combined. This 6-reading average was also used as the baseline BP for randomized participants. To examine the effects of intervention on participants already considered to have hypertension, a hypertensive stratum was defined as the subset of participants with untreated DBP of 90 to 99 mm Hg or who had had antihypertensive medication regimens discontinued to enter the trial and had a DBP of 80 to 99 mm Hg when not taking medication.

Screening exclusion criteria included alcohol or psychostimulant substance dependence, alcohol-attributed medical complications, major psychiatric diagnoses, cardiovascular end-organ damage, severe or secondary hypertension, malignancies, seizure disorders, coagulopathies, or current pregnancy. A participant who met the inclusion criteria was randomized to an intervention to reduce alcohol intake or to a control condition. An eligible participant was enrolled in the study by a telephone call to the coordinating center. Treatment assignments had been randomly determined at the start of the study using a fixed randomization scheme with uniform allocation, variable block size, and stratification by clinic. The study interventionist was notified by mail of the participant’s treatment group assignment.

The goal of the intervention was to reduce alcohol intake to the lesser of 14 drinks per week or 50% of the participant’s own baseline alcohol intake level. The intervention was administered by women from diverse disciplines (nursing, psychology, and social work) and with diverse educational and career histories, who were centrally trained in special intervention techniques. Interventionists were not involved in any postrandomization data collection. The intervention program was primarily a cognitive-behavioral program that included psychodynamic and interpersonal components and encouraged variation in the application of the model to meet an individual participant’s needs. The intervention consisted of 6 individual sessions during 3 months and a minimum of 3 sessions at monthly intervals for the remainder of the 6-month treatment phase. The maintenance phase lasted up to 18 months and consisted of a minimum of 6 visits at 1- to 3-month intervals.

Participants were followed for up to 2 years; the 95 participants randomized between October 1992 and June 1993 after the end of the originally scheduled intake period had final visits scheduled after 15 to 21 months. If SBP or DBP exceeded certain safety criteria, which have previously been published, open treatment of hypertension was initiated, with previous BP measurements used as the final outcome data, and the participant remained in the study. Participants who developed manifestations of alcohol dependence during the course of the trial continued in the study but were referred to an alcohol treatment program external to the trial.

The behavioral nature of the alcohol intervention necessitated an unmasked study design for the participant and the interventionist. Participants randomized to the control group were scheduled for data collection visits only. Particular care was taken to maintain blindness to intervention assignments among clinic personnel involved in collecting the primary study data common to both groups (data collectors), and to maintain blindness to BP and laboratory data among participants and interventionists. Data collection took place in the same location for both randomization groups, but participants in the alcohol intervention group were seen in a different location for...
intake could be achieved at 6 months and maintained.

The alcohol intake outcome measure, the Chronologic Drinking Record,19 was administered at the third screening visit and at 3, 6, 12, 18, and 24 months after randomization. It was an interviewer-assisted, retrospective diary of the participant's drinking on an event-by-event basis for the week before the data collection visit.

Biochemical markers for alcohol intake, γ-glutamyltransferase, high-density lipoprotein (HDL) cholesterol with HDL2 and HDL3 subfractions, apolipoproteins (Apo) A1 and A3, and carbohydrate-deficient transferrin were determined in the central lipid laboratory.20-22 Total cholesterol, low-density lipoprotein cholesterol, and triglyceride levels also were measured. These laboratory tests and a food frequency questionnaire23 were obtained at the same visits as the Chronologic Drinking Record. A timed overnight urine sample was collected for central determinations of sodium, potassium, magnesium, and creatinine levels, a physical activity questionnaire was administered, and a urine drug screen and other routine laboratory measurements were performed locally at 6, 12, 18, and 24 months after randomization.

Echocardiograms were performed during the baseline period and 6 months after randomization. Results are reported separately.

Study sample size was projected to be 566 (283 each group) to achieve 90% power for detecting a difference in SBP changes of 3 mm Hg between the 2 randomized groups (SD of change assumed to be 11 mm Hg) with a 2-sided statistical test and α = 0.03. Similarly, a total sample size of 316 was needed for detecting difference in DBP changes of 2 mm Hg (SD of change assumed to be 7 mm Hg). Total sample sizes for detecting differences of 4.5 mm Hg systolic and 3 mm Hg diastolic, respectively, in the hypertensive stratum were estimated to be 252 and 230. Based on these calculations, the sample size goal was set at 580 participants (290 each group) overall and at 260 participants (130 each group) for the hypertensive stratum.

The primary outcome measurements were changes in SBP and DBP through 6 months based on the assumption that many participants would require initiation of antihypertensive drug treatment beyond the 6-month visit. Blood pressure criteria for initiating antihypertensive drug treatment were lower beyond this point (≥95 mm Hg diastolic or ≥160 mm Hg systolic averaged during 3 consecutive weekly visits) in keeping with recommendations for beginning drug therapy for hypertension after 6 months if lifestyle interventions have not normalized BP.24 A 2-sample t test was used to determine if the change from baseline was significantly different between the 2 treatment groups. The analysis was performed using the intention-to-treat principle: all randomized participants with any follow-up data were included and final treatment BP was the average of BP at the last 2 monthly visits in the 6-month postrandomization period. For individuals receiving antihypertensive medication during the study, visits after initiation of medication were not used for determination of treatment BP. Only the BP at the final visit within the initial 6-month treatment phase was used if it occurred more than 2 months after the preceding visit, or if the final visit was within the first 3 months. Differences between the 2 treatment groups in the hypertensive stratum alone were also analyzed.

Repeated measures analyses also were performed to compare differences in BP between randomized groups using all BP determinations through the initial 6-month period as well as for the entire 24-month follow-up period. The BMDP5V software program was used for these repeated measures analyses.25 A simple regression model with no visit–treatment group interaction and an unstructured covariance matrix was used. Baseline BPWs were used as covariates. The BP readings from follow-up visits that occurred while participants were taking antihypertensive medication were not used in these analyses; instead, values from the most recent prior visit were carried forward. The same imputation procedure was used for most missed follow-up visits. The BP readings for visits that would have occurred after the death of a participant and for visits that did not occur because the study ended were considered missing.

Survival functions were used to evaluate the rate of development or recurrence of hypertension during follow-up. The product-limit method in SAS PROC LIFETEST was used for estimating survival curves.26

The success of the alcohol intervention program was evaluated using the self-reported retrospective diary data. Participants who had at least a 50% reduction in alcohol consumption between baseline and follow-up evaluation were labeled “successes”; those with less than a 50% reduction were labeled as “failures.” Participants with missing data were also labeled as “failures.” Between-group tests were performed using both the proportion of successes and changes in alcohol intake at the 6-month and 2-year evaluations. Success rates at 6 months were projected to be 60% in the intervention group and 20% in the control group; these success rates were assumed to produce a difference in the changes in alcohol intake of approximately 2 drinks per day between the 2 groups. These differences were assumed to be necessary to produce the predicted BP change differences.14 Similarly, success rates (30% and 10%) were projected for 2-year evaluations and the sample size was determined to be adequate for detecting such differences in alcohol intake.

Analysis of variance and χ2 techniques were used to detect statistically significant differences between treatment groups with regard to baseline characteristics. Two-sample t tests were used to determine if the changes from baseline for the biochemical markers were significantly different between the 2 treatment groups. To determine if there was evidence for differential levels of underreporting or overreporting of alcohol intake between the 2 treatment groups, changes in biochemical markers were analyzed using a 2-factor analysis of variance model. One factor was treatment group assignment. The second factor was a blocking factor and was determined by dividing participants into 5 approximately equally sized groups based on level of change in self-reported alcohol intake from baseline to the 6-month follow-up visit.

diastolic BP (DBP). To test for a BP effect, the trial also aimed to determine whether a reduction in alcohol intake could be achieved at 6 months and maintained for 2 years. This article reports the primary results of the Prevention and Treatment of Hypertension Study (PATHS).
RESULTS

SCREENING PHASE

Seven clinical sites collected brief screening instruments from 49,950 individuals: 41,425 were not further evaluated because they did not report consuming at least 10 drinks per week; 3386 were unwilling or unable to participate; 1212 were excluded because their BP was too low or too high at screening visits; 796 were excluded because they could not discontinue the contraindicated medication regimen; 633 were excluded for unknown reasons; 575 were excluded because they were dependent on alcohol; and 249 were excluded because their alcohol intake was too low. On completion of the 3-visit screening phase, 641 participants were eligible and entered the trial between April 1990 and June 1993. By randomization 320 were assigned to the alcohol intervention group and 321 to the control group. The hypertensive stratum included 266 (41.5%) of those randomized, 138 in the intervention group and 128 in the control group.

BASELINE CHARACTERISTICS

Baseline characteristics were not significantly different between randomized groups (Table 1). Participants averaged 57.3 years of age; 74.7% were white, 19.8% were African American, and 4.7% were Hispanic. Although both men and women were actively recruited, only 5 of the participants were women. Blood pressure averaged 140/86 mm Hg for all participants and 147/90 mm Hg for hypertensive participants; mean weight was 88 kg (mean body mass index, which is a measure of weight in kilograms divided by the square of the height in meters, was 28) and heart rate averaged 76/min. Alcohol intake averaged 6.0 drinks per day in the 6 months before randomization, although mean alcohol intake the week before randomization was 4.5 drinks per day (439 g/wk). Average duration of drinking was 37 years.

ALCOHOL INTAKE

Baseline alcohol intake for the 320 participants in the alcohol intervention group was 4.4 drinks per day. Alcohol intake at 24 months for 195 participants with 24-month data was 2.0 drinks per day. This represents a reduction of 2.3 drinks per day in this smaller cohort (Figure 1 and Table 2). Most of this reduction was observed by 3 months of follow-up. Baseline alcohol intake for the 320 participants in the control group was 4.5 drinks per day. The 212 participants with 24-month data reduced their alcohol intake by 1.1 drinks per day to 3.7 drinks per day. The differences between groups in changes from baseline were significant (P < .001) at each follow-up assessment and declined from a maximum of 1.8 drinks per day at 3 months to 1.2 drinks per day at 24 months (Table 2). Rates of success in reducing alcohol intake to 50% of a participant’s baseline level were also highly significantly different at each assessment; for
example, the success rates were 44% in the intervention group and 23% in the control group at 6 months. The alcohol intake results were similar for the hypertensive subgroup (Table 3), although the differences in reductions were larger. The treatment effect by repeated measures analysis averaged 1.3 drinks per day at 6 and 24 months. For the hypertensive stratum, the treatment effect averaged 1.6 drinks per day in the first 6 months and 1.4 drinks per day for 24 months.

**BIOCHEMICAL MARKERS**

The only significant differences between groups in changes in any of the biochemical markers (Table 4) were...
Table 4. Biochemical Markers of Alcohol Intake: Levels at Baseline and Changes at 3 and 6 Months in Intervention and Control Groups and Differences Between Groups

<table>
<thead>
<tr>
<th></th>
<th>Intervention (n)</th>
<th>Control (n)</th>
<th>Difference</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Apo A1, mg %</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>149.7 ± 1.6 (304)</td>
<td>152.5 ± 1.5 (308)</td>
<td>-2.8 ± 2.2</td>
<td>.21</td>
</tr>
<tr>
<td>Reduction at mo</td>
<td>3</td>
<td>4.7 ± 1.4 (246)</td>
<td>2.0 ± 1.3 (277)</td>
<td>2.7 ± 1.9</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>0.9 ± 1.3 (249)</td>
<td>0.6 ± 1.4 (273)</td>
<td>0.2 ± 1.9</td>
</tr>
<tr>
<td><strong>Apo A2, mg %</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>46.8 ± 0.6 (304)</td>
<td>46.4 ± 0.6 (309)</td>
<td>0.4 ± 0.8</td>
<td>.66</td>
</tr>
<tr>
<td>Reduction at mo</td>
<td>3</td>
<td>3.6 ± 0.7 (247)</td>
<td>1.7 ± 0.7 (277)</td>
<td>2.0 ± 1.0</td>
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<tr>
<td></td>
<td>6</td>
<td>2.4 ± 0.7 (249)</td>
<td>1.7 ± 0.7 (270)</td>
<td>0.7 ± 1.0</td>
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<tr>
<td><strong>GGT, U/L</strong></td>
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<tr>
<td>Baseline</td>
<td>58.4 ± 3.8 (304)</td>
<td>56.2 ± 3.3 (309)</td>
<td>2.3 ± 5.1</td>
<td>.65</td>
</tr>
<tr>
<td>Reduction at mo</td>
<td>3</td>
<td>-1.0 ± 3.6 (248)</td>
<td>-3.6 ± 1.7 (278)</td>
<td>2.6 ± 3.9</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>4.8 ± 2.5 (249)</td>
<td>-1.6 ± 2.0 (273)</td>
<td>6.5 ± 3.2</td>
</tr>
<tr>
<td><strong>HDL, mg %</strong></td>
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<tr>
<td>Baseline</td>
<td>50.7 ± 0.8 (304)</td>
<td>52.4 ± 0.9 (307)</td>
<td>-1.7 ± 1.1</td>
<td>.14</td>
</tr>
<tr>
<td>Reduction at mo</td>
<td>3</td>
<td>2.4 ± 0.8 (248)</td>
<td>2.1 ± 0.6 (278)</td>
<td>0.3 ± 1.0</td>
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<tr>
<td></td>
<td>6</td>
<td>0.9 ± 0.8 (249)</td>
<td>2.3 ± 0.7 (273)</td>
<td>-1.4 ± 1.0</td>
</tr>
</tbody>
</table>

*Values are mean ± SE. Apo indicates apolipoprotein; GGT, γ-glutamyltransferase; and HDL, high-density lipoprotein.

Apo A2 at 3 months and γ-glutamyltransferase at 6 and 12 months (data not shown for 12 months). When changes for HDL, HDL3, Apo A1, Apo A2, and γ-glutamyltransferase were compared between participants successful in achieving a 50% reduction in alcohol intake with those not successful, most differences were significant overall and within each randomized group. When changes in biochemical markers were analyzed with quintiles of change in self-reported alcohol intake used as a blocking factor, there were no statistically significant differences between the intervention and control groups (Figure 2). In general, the greater the reduction in alcohol intake reported, the greater the average reduction in the biochemical marker. The correlation between change in reported alcohol intake (Chronicologic Drinking Record) at 6 months and changes in markers were all positive and the Pearson correlation coefficients for Apo A1 (r = 0.24) and Apo A2 (r = 0.20) were statistically significant (P < .001 for both).

**BLOOD PRESSURE**

Average BP at each time period by treatment group is displayed in Figure 3 for all participants and for the hypertensive stratum. At most time points, mean levels were lower in the intervention group. For the entire study, the larger differences in BP change from baseline were seen at 3, 12, and 24 months, significantly greater in the intervention group for DBP at 12 and 24 months (Table 5). For the hypertensive stratum the only significant difference was for SBP at 3 months (Table 6).

Treatment BP, as defined previously, was available for 622 participants (97% of those randomized); it could not be determined for 19 participants who either failed to return for any follow-up visits or were started on a regimen of antihypertensive medication before their first follow-up visit. Treatment BP was the average of the 5- and 6-month visits for 415 participants (65% of those randomized). For the entire study cohort, the intervention group had a 1.2/0.7 mm Hg greater reduction in BP than the control group (for each, P = .17 and P = .18) for the 6-month primary end point. For the hypertensive stratum the BP difference was 0.9/0.7 mm Hg (for each, P = .58 and P = .44). For the entire cohort, the power to detect a difference of this magnitude in this study was 27% for both SBP and DBP. For the hypertensive stratum, the power to detect differences of this magnitude was 8% for SBP and 12% for DBP. When all visits through 6 months of follow-up were taken into account with repeated measures analysis (Table 5), the effect size was 1.0/0.6 mm Hg (for each, P = .11 and P = .09); for 24 months it was 0.9/0.6 mm Hg (for each, P = .16 and P = .10). The effect size by repeated measures analysis for the hypertensive stratum (Table 6) was 1.9/0.6 mm Hg (for each, P = .08 and P = .33) over the first 6 months and 1.6/0.4 mm Hg (for each, P = .13 and P = .51) over 24 months.

**WEIGHT, URINARY ELECTROLYTES, DIET, AND PHYSICAL ACTIVITY**

Weight declined slightly more in the intervention group than in the control group, eg, by 0.5 kg at 6 months (P < .05) and 1.0 kg at 24 months (P = .06). Changes in overnight urinary excretion of sodium, potassium, and magnesium were not significantly different between the intervention and control groups. From food frequency questionnaires, there were no significant differences for calcium intake in changes from baseline. However, intake of saturated fat decreased about 3 to 4 g more in the intervention than the control participants at 18 and 24 months, respectively (P < .05 for both). There were no significant differences in physical activity levels between groups.

**INCIDENCE OF HYPERTENSION**

All participants were considered to be at risk for either new or recurrent hypertension at enrollment. Hypertension occurred whenever antihypertensive medication was initiated for a diagnosis of hypertension or whenever one of the BP escape criteria15 were met regardless of whether medication was initiated. By the end of follow-up (24 months), 16.6% of participants in the intervention group and 21.8% of participants in the control group were being treated for hypertension or had met BP escape criteria but were not being treated. The product-limit estimates of the 2-year hypertension incidence rate were 21.4% and 25.7% for intervention and control groups, respectively. These differences are not statistically significant (P = .28). There also were no significant differences between the intervention and control groups in the observed or estimated hypertension recurrence for the baseline hypertensive stratum (29.3% vs 37.5%, and 37.3% vs 45.7%, respectively), or in the observed or estimated
incidence of hypertension for the nonhypertensive stratum (7.7% vs 11.4%, and 9.8% vs 13.4%, respectively).

OTHER EVENTS

There were 6 deaths in the intervention group and 5 in the control group. Acute myocardial infarction was the cause of 4 deaths in the intervention group and 2 deaths in the control group; another death in the control group was from possible coronary heart disease. One death in the intervention group was the result of a cerebral hemorrhage. Cancer was the cause of 1 death in each treatment group. The remaining death in the control group was caused by bronchial asthma.

Fatal or nonfatal acute myocardial infarction occurred in 6 intervention and 2 control participants. Four intervention and 10 control subjects experienced cardiac dysrhythmia. Three from the intervention group developed congestive heart failure compared with 2 control subjects. Three subjects from the intervention and 1 from the control groups experienced strokes. In addition, 2 subjects from the intervention and 1 from the control groups had transient ischemic attacks. Overall, cardiovascular events occurred in 18 intervention and 17 control participants.

COMMENT

In this randomized clinical trial in nondependent moderate to heavy drinkers the reduction in BP with an intervention to lower alcohol intake was not significantly different from the BP change in a control group. The BP differences and the development or recurrence of hypertension are generally in the hypothesized direction, but they do not achieve statistical significance.

There are several possible explanations for the lack of significant treatment effect seen in PATHS. These include (1) lack of a true relationship between change in alcohol intake and change in BP, (2) a weaker dose-response relationship between change in...
alcohol and BP than had been expected, and (3) a less-than-expected effect of intervention on change in alcohol intake. These possibilities are each considered in the following paragraphs.

The possibility that there is no true relationship between alcohol intake and BP would contradict a large body of evidence, including at least 32 observational studies and at least 10 randomized trials.11,27 Most of the clinical trials were relatively small and of short duration; baseline levels of alcohol intake and changes in alcohol intake were generally larger than what we observed in PATHS.11 The net reductions in BP were usually significant, averaging up to 8 mm Hg systolic and up to 6 mm Hg diastolic, for differences in alcohol intake of 1 to 6 drinks per day. One of these trials was of identical size to PATHS and of 1-year duration, but the intervention was less intense and only achieved a difference in average reduction in reported alcohol intake of 1.0 drink per day.28 Nevertheless, the 2.1–mm Hg net SBP reduction was reported as significantly greater (P < .05) in the intervention group.

A second possible explanation for the lack of a significant result in PATHS is that the dose-response relationship between change in alcohol consumption and change in BP is weaker than had been thought. Among the studies reported in the literature, 2 studies by Puddey et al in normotensive men29 and subjects with hypertension30 are probably the best from which to derive a crude prediction for BP change based on the alcohol change observed in PATHS. Averaging over the 2 studies, a 3.0-drink per day net reduction was associated with a 4.4/2.2–mm Hg reduction in BP. If one assumes a linear relationship with a zero intercept (no change in alcohol intake results in no change in BP), the studies by Puddey et al would suggest a 1.9/

### Table 5. Blood Pressure Levels at Baseline and Changes During 24 Months in Intervention and Control Groups, Differences Between Groups, and Repeated Measures Treatment Effects for All Participants*

<table>
<thead>
<tr>
<th></th>
<th>Systolic Blood Pressure</th>
<th>Diastolic Blood Pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intervention (n)</td>
<td>Control (n)</td>
</tr>
<tr>
<td>Baseline</td>
<td>139 ± 0.8 (320)</td>
<td>140.5 ± 0.8 (321)</td>
</tr>
<tr>
<td>Reduction at mo</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>5.4 ± 0.7 (251)</td>
<td>3.6 ± 0.7 (284)</td>
</tr>
<tr>
<td>6</td>
<td>5.9 ± 0.6 (248)</td>
<td>4.8 ± 0.6 (260)</td>
</tr>
<tr>
<td>12</td>
<td>6.3 ± 0.9 (200)</td>
<td>4.2 ± 0.8 (236)</td>
</tr>
<tr>
<td>18</td>
<td>5.7 ± 0.9 (183)</td>
<td>4.8 ± 0.9 (208)</td>
</tr>
<tr>
<td>24</td>
<td>5.3 ± 1.0 (157)</td>
<td>3.4 ± 0.8 (168)</td>
</tr>
<tr>
<td>Repeated measures</td>
<td></td>
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<tr>
<td>treatment effect at 6</td>
<td>. . . . . . . . . . . . . . .</td>
<td>. . . . . . . . . . . . . . .</td>
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<tr>
<td>24</td>
<td>. . . . . . . . . . . . . . .</td>
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</tbody>
</table>

* In the repeated measures analyses, blood pressure values have been imputed when measurement data were not available. Values are mean ± SE. Ellipses indicate not applicable.

### Table 6. Blood Pressure Levels at Baseline and Changes During 24 Months in Intervention and Control Groups, Differences Between Groups, and Repeated Measures Treatment Effects for Participants in the Hypertensive Stratum*

<table>
<thead>
<tr>
<th></th>
<th>Systolic Blood Pressure</th>
<th>Diastolic Blood Pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intervention (n)</td>
<td>Control (n)</td>
</tr>
<tr>
<td>Baseline</td>
<td>145.5 ± 1.1 (138)</td>
<td>147.7 ± 1.1 (128)</td>
</tr>
<tr>
<td>Reduction at mo</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>6.5 ± 1.0 (109)</td>
<td>3.0 ± 1.1 (115)</td>
</tr>
<tr>
<td>6</td>
<td>5.2 ± 1.4 (106)</td>
<td>5.4 ± 1.3 (104)</td>
</tr>
<tr>
<td>12</td>
<td>7.4 ± 1.4 (82)</td>
<td>4.4 ± 1.6 (80)</td>
</tr>
<tr>
<td>18</td>
<td>5.5 ± 1.7 (70)</td>
<td>7.0 ± 1.8 (64)</td>
</tr>
<tr>
<td>24</td>
<td>5.5 ± 2.1 (53)</td>
<td>4.7 ± 1.7 (44)</td>
</tr>
<tr>
<td>Repeated measures</td>
<td></td>
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<tr>
<td>treatment effect at 6</td>
<td>. . . . . . . . . . . . . . .</td>
<td>. . . . . . . . . . . . . . .</td>
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<tr>
<td>24</td>
<td>. . . . . . . . . . . . . . .</td>
<td>. . . . . . . . . . . . . . .</td>
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</tbody>
</table>

* In the repeated measures analyses, blood pressure values have been imputed when measurement data were not available. Values are mean ± SE except where otherwise indicated. Ellipses indicate not applicable.
1.0–mm Hg change in BP for PATHS. While both are within 1 SD of the 1.2/0.7–mm Hg effect seen in PATHS, the prediction is somewhat larger. This suggests that linear predictions based on relatively larger differences in alcohol change may be overly optimistic when extrapolated to relatively small differences in alcohol intake. Thus, a weaker dose-response relationship for the relatively small changes in alcohol intake seen in PATHS and a stronger dose-response relationship for larger changes in intake remains a possible explanation. Another possibility is that while the true relationship is linear, intervention subjects in PATHS overreported reductions in alcohol intake relative to the control group. If true, the actual difference would be less than the 1.3-drink per day difference reported. Our investigation of potential differential self-report based on the relationship between changes in reported alcohol intake and changes in biochemical markers (Figure 2) showed no clear evidence for differential reporting bias. This does not rule out the possibility of equal reporting bias in both randomized groups. Further study of the dose-response relationship within the PATHS cohort is planned.

The most likely explanation for the lack of significant effects on BP in PATHS is lack of a sufficient between-group difference in alcohol change. The PATHS was designed based on the expectation of a 2-drink per day difference between treatment groups at 6 months.31 However, only about two thirds of this difference (1.3 drinks per day) was achieved. Meaningful effects on BP may require larger than the 1.3-drink per day between-group difference in alcohol consumption. Indeed, a meaningful change in BP may result only at the magnitude of difference in alcohol consumption found in the studies outlined above.31 Although these differences were 2 to 4 times the magnitude seen in PATHS, the methods for reducing alcohol intake differed from those used in PATHS and may not be suitable for longer-term, sustained lifestyle change.

The behavioral intervention used in PATHS failed to produce the anticipated reduction in BP. In the studies by Puddey et al,29,30 beer was substituted with low-alcohol beer in the intervention groups while the control groups continued drinking regular beer.29,31 Using the studies by Puddey et al as a comparison, one might find that for subjects similar to those studied herein reductions in alcohol intake that rely less on self-management and more on a substitute for the form of alcohol consumed may be a better method for achieving significant differences in BP reduction, at least in a clinical trial. However, beverage substitution may not be a satisfactory method to use over an extended period. The results from PATHS are probably a more realistic expectation for sustained reduction in alcohol intake among nondependent moderate drinkers in a natural setting. There is a suggestion that reduction of alcohol intake in the control group in PATHS attenuated the difference in intake between the 2 groups. The difference in the proportion of participants reporting successfully reducing alcohol intake to less than 50% of their baseline intake was less than had been estimated to produce a sufficient difference in alcohol intake and BP for this sample size. The projection was 60% for the intervention group and 20% for the control group at 6 months, while levels of 44% and 23%, respectively, were achieved. Alternatively, self-report may have overestimated the actual alcohol intake reductions in both groups. Detailed examination of the intervention and its effects on alcohol intake is planned.

Although the differences in biochemical marker changes between randomized groups were neither large nor consistent, the changes between participants within each group who were successful in reducing their alcohol intake to at least 50% of baseline intake vs those who failed to do so corroborated changes in alcohol intake. In addition, correlations between change in reported alcohol intake (Chronologic Drinking Record) at 6 months and changes in markers were all positive and the correlation coefficients for Apo A1 and Apo A2 were statistically significant (P < .001 for both). A more complete analysis of the biochemical markers will be the subject of another article; however, markers have been useful mainly in providing general corroborative data, particularly by distinguishing heavier drinkers from others, in studies32 in which drinking is the dependent variable. In addition, the sensitivity and specificity of biochemical markers falls in the low to moderate range, at the lower end for moderate nondependent drinkers such as those in PATHS. They are also effective within a limited time frame and are susceptible to effects of age, tobacco, exercise, diseases, and drugs.33

There was little evidence that changes in weight, sodium or potassium intake, other dietary factors, or physical activity confounded the effect of a change in alcohol intake on BP, although there were small decreases in body weight and saturated fat intake.

The degree of reduction in self-reported alcohol intake observed in this trial by an average of 1.3 drinks per day was associated with only small nonsignificant effects on BP in the hypothesized direction. Greater differences in alcohol reduction may have resulted in greater differences in BP reduction. The 1997 Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC VI)34 from the National Heart, Lung, and Blood Institute recommended that alcohol intake should be limited to no more than 1 to 2 drinks per day for the prevention or treatment of hypertension. Some evidence suggests that, compared with abstention, alcohol intake not exceeding these levels may reduce atherosclerotic events, such as myocardial infarction and atherothrombotic strokes, apparently at least in part because of the beneficial effects on protective lipoproteins and platelet aggregability.34-37 However, higher intake levels are discouraged because of increased risk for hypertension, cardiomyopathy and other cardiac complications, certain kinds of cancer, liver damage and other gastrointestinal complications, suicides, accidents, and alcohol abuse and dependence.34,38
The results of PATHS should not alter recommendations that individuals with, or at risk of, hypertension should consume no more than an average of 1 to 2 drinks per day. We recommend moderation in alcohol intake as part of a multifactor intervention, but it should not preempt other lifestyle changes, such as weight loss or sodium reduction. The results of PATHS also suggest that there is a need for more research on behavior change methods. In addition, more research is needed on biochemical indexes as markers for change in alcohol intake within the range studied herein.

In conclusion, in this randomized clinical trial in nondependent moderate to heavy drinkers, the difference in the reduction in BP with an intervention to lower alcohol intake compared with a control group was small and not significant. Greater differences in alcohol reduction may have resulted in greater differences in BP reduction. The PATHS results are consistent with the antihypertensive effect seen in well-controlled short-term studies that observed a greater difference in alcohol intake between randomized groups. However, the results from PATHS do not lend strong support for reduction of alcohol consumption in nondependent moderate drinkers to no more than 2 drinks per day as a unifactorial approach for the prevention or treatment of hypertension.

Accepted for publication October 16, 1997.

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REFERENCES