Recruitment for Phase I of the Trials of Hypertension Prevention

II - 10

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Phase I of the Trials of Hypertension Prevention was a multicenter, randomized, controlled trial designed to determine the efficacy of seven nonpharmacologic interventions in reducing blood pressure among persons with high-normal diastolic blood pressure. The initial goal for recruitment was to enroll 2,100 participants over a nine-month period. The two major strategies for reaching potential participants were direct mailings and work site screenings. The yield from the first screening visit to randomization was 13% overall, with clinic-specific yields ranging from 4.5% to 31.7%. After five months of recruitment, approximately 60% of the goal for that point in the recruitment timetable had been randomized. Clinical centers falling short of their goals at that time altered their recruitment strategies and intensified their efforts, and centers that had exceeded their goals recruited additional participants. As a result, 2,182 participants, or 104% of the goal for recruitment, were randomized over a 13-month period. Those clinics using a cohort, or wave, type of enrollment were most successful in achieving their recruitment goals within the prescribed timetable. [Am J Prev Med 1993;9:237–43]

Recruitment for a clinical trial poses many challenges, even to experienced investigators and recruitment staffs. Each clinical trial presents unique recruitment problems, but much can be learned from experience in previous studies. A review of the recruitment experience for Phase I of the Trials of Hypertension Prevention (TOHP) offers an opportunity to examine recruitment for a national trial of primary prevention of hypertension. Although recruitment for Phase I of TOHP was difficult, the ultimate success of the recruitment methods used could provide insight in planning recruitment for future clinical trials.

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METHODS

Trial design and aims of the study. Phase I of TOHP was a multicenter, randomized, controlled clinical trial. Its primary aims were to assess the short-term efficacy of selected nonpharmacologic interventions in the prevention of an increase in diastolic blood pressure (DBP) in individuals with high-normal DBP (i.e., 80–89 mm Hg) and to assess the feasibility of conducting a long-term trial of hypertension prevention. The lifestyle change arm of the study examined the effects of weight reduction, stress management, and sodium restriction over 18 months of follow-up. These intervention programs were delivered through small-group (8–15 participants) and individual counseling sessions. The results in the three lifestyle change groups were each compared to corresponding results in unmasked, nonintervention controls. The nutritional supplement arm of the study used a double-blind, placebo-controlled design, in which the initial randomization (stage 1) was assignment to calcium, magnesium, or placebo. After a wash-out period, participants were randomized to a stage 2 supplement program, consisting of potassium, fish oil, or placebo. Each stage of the nutritional supplement arm lasted six months.

The TOHP study design was complex because of the diversity of the interventions evaluated. The 10 participating clinical centers tested the various interventions in the following manner: three clinics offered only two of the lifestyle change interventions, two clinics offered only nutritional supplements, and five "hybrid" clinics offered both lifestyle and supplement interventions. The choice of interventions administered by each clinic was determined by the availability of staff with experience in the various intervention areas. A complete description of the TOHP design has been published elsewhere.[1] Consult Appendix 1 for a list of the TOHP participating institutions and principal staff.

Eligibility criteria and screening visits. The eligibility and exclusion criteria for TOHP recruitment were chosen to select a group of healthy, nonhypertensive individuals who could be randomized safely to any of the intervention groups and who would be likely to comply with the treatment program and follow-up visit schedule. Men and women 30–54 years of age were considered potentially eligible, regardless of ethnicity or race. Candidates with an average DBP <79 or ≥90 mm Hg (based on nine readings over three visits using a random zero sphygmomanometer) were excluded, as were those with a history of taking antihypertensive medications during the two months prior to screening. Also, individuals with a body mass index (BMI) greater than or equal to approximately 36 kg/m^2 (0.0514 lb/in^2) or approximately 160% of ideal body weight were excluded. Additional exclusion criteria appear in Appendix 2.

The screening phase consisted of three clinic visits to determine eligibility. Blood pressure (BP) was measured at these screening visits by trained, certified observers according to a uniform protocol. DBP eligibility criteria were chosen for each of the three screening visits according to a predictive value screening rule designed so that at each visit those excluded had ≥80% chance that their true DBP would fall outside the final eligibility range of 80–89 mm Hg.[1,2] At each of the three screening visits, DBP was determined as an average of all screening DBPs obtained up to that time (three per visit). The candidate's overall average DBP had to fall within the following ranges to achieve eligibility for the next visit: screening visit 1 (SV1): DBP 75–97 mm Hg (3 readings); screening visit 2 (SV2): DBP 77–94 mm Hg (6 readings); screening visit 3 (SV3): DBP 80–89 mm Hg (9 readings). In addition to determination of eligibility, the screening visits allowed assessment of a candidate's willingness to comply with the visit schedule and the behavioral modifications necessary for implementation of the interventions and willingness to accept randomization into any of the potential intervention arms, including the nonintervention control group.

Further, a candidate's willingness and ability to complete a food frequency questionnaire and 24-hour urine collections were evaluated at an additional visit, the status review visit (SRV), prior to actual randomization. At the hybrid clinics, candidates initially received a preliminary random assignment either to the lifestyle change or to the nutritional supplement arm of the trial. Potential participants in the nutritional supplement arm were enrolled in a six-week run-in phase in which they took nutritional supplement placebos. Only those candidates who successfully completed the run-in phase by taking 60% or more of the assigned pills, as determined by pill counts, were eligible for randomization to the supplement interventions.

Recruitment goals. A total sample of 2,100 participants (200 at each lifestyle or hybrid clinic and 250 at each nutritional supplement clinic) was the goal for recruitment. This sample size was expected to allow detection of a 1.6 mm Hg net change in DBP and a 2.5 mm Hg net change in systolic blood pressure (SBP) with at least 80% power, at a significance level of .05, for each intervention-control comparison.[1,3] The original goal was to recruit these 2,100 participants during a nine-month period, beginning August 1, 1987. Table 1 lists the 10 TOHP clinics, the type of clinic (i.e., lifestyle, supplement, or hybrid), and the initial goal, as well as the actual number randomized, for each clinic.

Prescreening. TOHP clinical centers undertook various activities to identify potentially eligible candidates for the trial, prior to the initial screening visit. There was no standardized, trial-

Table 1. Expected and actual clinic allocations for lifestyle and stage 1 supplement interventions

Clinic	Sodium restriction expected/ actual	Weight reduction expected/ actual	Stress management expected/ actual	Control group expected/ actual	Calcium expected/ actual	Magnesium expected/ actual	Placebo expected/ actual	Total expected/ actual
Baltimore	60/66	60/60	—[a]	80/82	—/22	—/20	—/21	200/289[b]
Birmingham	—	60/63	60/66	80/89	—	—	—	200/218
Davis	45/69	45/45	—	60/83	17/51	17/48	16/50	200/346
East Boston	—	—	—	—	83/23	83/22	84/22	250/67
Jackson	45/49	45/42	—	60/67	17/17	17/14	16/16	200/205
Memphis	45/47	—	45/50	60/63	17/21	17/22	16/22	200/225
Newark	60/63	—	60/66	80/85	—	—	—	200/214
Pittsburgh	—	—	—	—	83/92	83/90	84/91	250/273
Portland	—	60/60	60/60	80/83	—	—	—	200/209
St. Louis	45/33	45/32	—	60/37	17/11	17/11	16/12	200/136
Total	300/327	315/308	225/242	560/589	234/237	234/227	232/234	2,100/2,182

[a]Dash indicates not applicable or none expected.
[b]Eighteen participants were randomized directly to stage 2 supplement arm in Baltimore.

wide prescreening procedure, however. The prescreening procedures could be classified into two categories: (1) telephone interviews using a checklist to determine if the screenee met basic eligibility criteria for the trial, and (2) a field prescreen before SV1 using a similar checklist, including a casual BP measurement, using a standard mercury sphygmomanometer. A DBP in the range of 74–102 mm Hg at prescreen was recommended for eligibility to attend SV1.

Recruitment activities. Early in the planning stage of the trial, each clinical center identified a recruitment coordinator to direct the recruitment effort. Staffing for the recruitment effort varied from center to center, but generally fell into two patterns. Two clinics had a separate team charged with recruitment of study participants and scheduling of initial appointments. Others used their general clinical center staff for those tasks. The staffing requirements for recruitment activities were approximately two to two and one-half full-time equivalents (FTEs) at each center.

A study-wide brochure and logo were developed with the help of the Public Information and Resources Branch, National Heart, Lung, and Blood Institute (NHLBI). The brochure design was based on marketing and direct mailing concepts and included a postage-paid response card that could be returned to the respective TOHP clinic. The study-wide brochure was designed to avoid duplication of effort at each of the 10 TOHP centers, as all centers had expressed the desire to use a brochure of some sort in their recruitment efforts. Clinical centers modified the brochure to include clinic-specific information.

Three of the eight clinical centers conducting lifestyle change interventions (Baltimore, Davis, and Memphis) used a cohort, or wave, approach to recruitment, whereas the other five clinics conducting lifestyle interventions employed a continuous recruitment approach. With the cohort approach, specific randomization goals were set for each wave of mass mailing or work-site screening. Recruitment in cohorts also allowed the scheduling of screening visits in waves, so that all screening visits of a certain type for a cohort could be completed in a specified period of time. The cohort recruitment model was also chosen to avoid a long lag time between randomization and the initiation of intervention activities in small groups. The two clinics conducting only the nutritional supplement intervention chose to use a continuous recruitment model, since group formation was not a concern.

Multiple recruitment strategies were used in reaching potential candidates for TOHP. Some clinical centers concentrated primarily on one approach, supplemented to varying degrees by other methods as the recruitment period grew shorter. Most of the efforts, however, could be classified into the following four categories:

1. Direct mailing: each center used some type of direct mailing. At seven centers, direct mailing was the primary strategy for recruitment. The source list for the mailings included voter registration rolls, motor vehicle registration and driver license lists. Other sources included lists of employee groups, health maintenance organization (HMO) subscribers, as well as screenees from previous trials. Generally, the mailing consisted of a TOHP brochure and a letter containing an invitation from the principal investigator or senior staff member to consider participation in the study. The contents of the mailing, the extent of personalization of the letters, and the methods of addressing the envelopes varied across clinics. At three centers, some of the mailings were followed by telephone calls from the clinic staff to encourage potential screenees to make appointments for initial screening visits. These mailings followed by telephone calls were, for the most part, to persons on lists that included telephone numbers, such as lists of university employees, HMO subscribers, patients at a neighborhood health clinic, and persons enumerated in a census of the area served by that clinic.

2. Work-site screening: eight clinical centers used some type of work-site screening. This was the primary strategy at two of the TOHP clinical centers (Baltimore and St. Louis). Both of these clinics marketed the TOHP objectives successfully to management and employee groups of local businesses with large employee bases. TOHP was identified as a primary prevention study that could benefit their employees. Each of these centers began negotiations with employer and employee representatives many months before the actual screening took place, and the negotiations required numerous meetings and telephone calls. For centers that focused their recruitment efforts at work sites, clinics at or near the work site were arranged.

3. Publicity: eight clinical centers used some form of promotion aimed at publicizing the study to the general public. These activities included paid and nonpaid advertising (news stories and TV and radio talk shows) and the use of posters and brochures in public areas.

4. Community screening: Eight clinical centers used some form of mass community screening in an effort to reach the public in their catchment areas. Screening was conducted at businesses serving the public, at health fairs, at churches and at civic groups, clubs, and organizations. In most centers, this type of screening was an adjunct to other recruitment strategies.

RESULTS

Screening for TOHP began in August 1987, and the first randomization occurred in September 1987. Initially, the goal was to complete screening visits by May 1988 and randomizations by June 1988 for the lifestyle participants and by August 1988 for the supplement participants. Figure 1 presents the actual number of randomizations compared with the goal. By the end of February 1988, or the fifth month of recruitment, the actual number of randomizations represented only 60% of the goal for that point in the recruitment phase. To correct this lag in enrollment, a series of semimonthly conference calls were initiated with the principal investigators of the clinics that had not met their recruitment goals, the chairman of the eligibility and recruitment subcommittee, the NHLBI project officer, and representatives from the coordinating center staff to monitor recruitment activities and to develop procedures to improve enrollment. In addition, recruitment problems were addressed during site visits to four of the clinical centers, and letters of encouragement were sent to the principal investigators on behalf of the trial's data and safety monitoring committee. Also, the period for randomization was extended to July 1988 for lifestyle participants and to October 1988 for supplement participants.

In May 1988, it was apparent that two clinics would not meet their goals, and three clinics (Baltimore, Davis, and Memphis) agreed to recruit additional participants to meet the goal for the trial as a whole. Baltimore became a hybrid clinic and

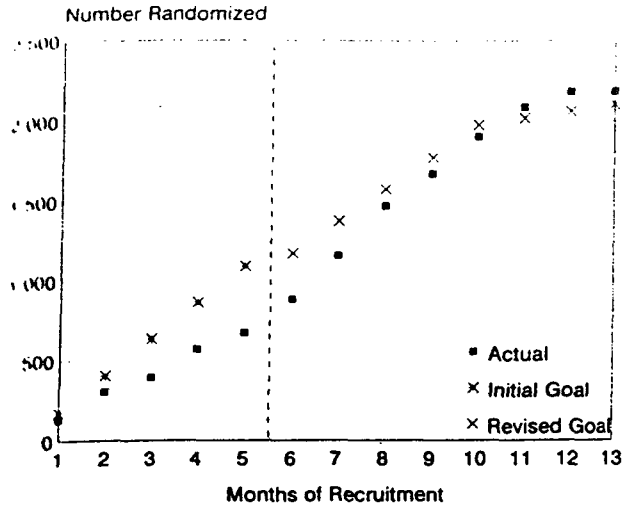

Figure 1. TOHP randomizations compared to goal.

randomized additional participants into the nutritional supplement arm. Davis increased allocations to the sodium restriction, lifestyle control, and supplement groups, and Memphis increased allocations across all its intervention groups (Table 1). At the end, 2,182 participants, or 104% of the goal of 2,100, were randomized by October 1988, resulting in a total randomization period of 13 months (Figure 1). The randomization goals for each intervention group were exceeded, except for weight reduction and magnesium supplementation, for which 97% to 98% of the goals were achieved.

Screening results by clinic appear in Table 2. The yield from SV1 to randomization for TOHP overall was 13%. The yields at each clinic varied widely, ranging from 4.5% in East Boston to 31.7% in Baltimore. This variation in percentage randomized among the clinical centers may reflect, to a certain extent, the differences in target populations and prescreening procedures across the centers. The low yield in East Boston may be attributable to its initial target population, patients of a neighborhood health clinic. Many of these potential participants were excluded because of medical history. In Baltimore, the focus on prescreening of employees at a work site may account for the high yield. However, in St. Louis, similar prescreenings in the work site were less productive, probably because of scheduling difficulties. The percentage of candidates who were prescreened with a blood pressure measurement before SV1 varied from 0.5% to 99.5%.

Overall, prescreening that included a BP measurement resulted in a higher SV1 eligibility rate and a slightly higher randomization rate. For candidates who were prescreened with a BP measurement, the SV1 eligibility rate was 60%, and the randomization rate was 15%. For those who were not prescreened, the SV1 eligibility rate was 46%, and the randomization rate was 12%. The primary reason for ineligibility at each screening visit was average DBP outside the eligibility range. At SV1, 36% of the screenees had DBP outside the eligibility range; at SV2 and SV3, these percentages were 26% and 39%, respectively. Approximately 1% of the screenees at each screening visit were excluded because of unwillingness to continue. Other reasons for ineligibility included medical history, weight, use of medications or nutritional supplements, and lack of compliance, demonstrated by failure to complete food frequency questionnaires, to collect 24-hour urine specimens, or, for potential supplement participants, to take at least 60% of the pills in the run-in period.

As shown in Table 3, the yield from direct mailing in terms of contacts, responses, or appointments varied from 1% to 7% across the clinics. The number of letters mailed at Davis and Portland include second mailings, and the response rate is based on the total number of letters mailed. In East Boston, 4,980 telephone contacts followed mailings to patients registered at the neighborhood health center or persons enumerated in a census of East Boston residents. In Portland, there were 23,411 telephone call attempts to reach HMO subscribers who had received letters. In Pittsburgh, university employee lists, which included telephone numbers, were used for most of the follow-up calling, and some calling was conducted using a reverse directory to obtain telephone numbers. Follow-up calling was time-consuming, particularly if lists included incorrect or out-

Table 2. Report on screening and randomization in Phase I of TOHP, percentage eligible by visits and clinic

Clinic	% of initial screening visits prescreened	Screening visit 1			Screening visit 2			Screening visit 3				
		Visits *n*	Eligible *n*	% eligible	Visits *n*	Eligible *n*	% eligible	Visits *n*	Eligible *n*	% eligible	Number randomized	Overall[a] % randomized
Baltimore	70.9	912	682	74.8	609	498	81.8	471	316	67.1	289	31.7
Birmingham	5.7	1,401	808	57.7	654	486	74.3	429	240	55.9	218	15.6
Davis	0.5	4,229	1,758	41.6	1,540	937	60.8	819	378	46.2	346	8.2
East Boston	28.5	1,493	469	31.4	419	254	60.6	205	80	39.0	67	4.5
Jackson	31.0	983	605	61.6	524	387	73.9	346	218	63.0	205	20.9
Memphis	24.7	1,819	922	50.7	715	547	76.5	487	259	53.2	225	12.4
Newark	21.0	1,016	631	62.1	561	431	76.8	391	238	60.9	214	21.1
Pittsburgh	71.7	1,707	947	55.5	789	594	75.3	544	305	56.1	273	16.0
Portland	99.5	2,176	1,288	59.2	1,076	660	61.3	577	241	41.8	209	9.6
St. Louis	98.5	1,085	543	50.1	475	315	66.3	291	142	48.8	136	12.5
Total	39.2	16,821	8,653	51.4	7,362	5,109	69.4	4,560	2,417	53.0	2,182	13.0

[a] Percentage randomized of total number of first screening visits.

Table 3. Results of mailings by clinic

Clinic	Number of letters mailed	% Responses	% of total number of initial screening visits	% of total randomized
Baltimore	43,340	3	31	17
Birmingham	24,100	2	25	25
Davis	193,799[a]	6	98	98
East Boston[b]	61,700	2	62	55
Jackson	82,539	3	83	69
Memphis	152,677	3	78	78
Newark	69,841	4	50	—[c]
Pittsburgh[b]	140,000	1	70	70
Portland[b]	101,638[a]	7	100	100
St. Louis	30,000	2	11	—

[a]Includes second mailings.
[b]Mailings were followed by telephone calls by clinic staff to encourage candidates to schedule appointments for initial screening visit.
[c]Dash indicates figures are not available.

dated numbers or when numbers had to be obtained from a reverse directory, but such calling was considered a necessary additional strategy to increase the number of screening appointments. At seven of the clinical centers, mailings resulted in 50% or more of the total number of SV1s. In most clinics, the percentage of the total number of randomizations resulting from mailings was similar to the percentage of SV1s from mailings. However, in Baltimore, East Boston, and Jackson, those recruited by mailings contributed less to the total number randomized than they did to the total number of SV1s.

Work-site screening was conducted at eight centers (Table 4). In Baltimore and St. Louis, screenings at the work site accounted for more than two thirds of the SV1s. The percentage of total number of randomizations from work-site screenings was slightly higher than the percentage of total number of SV1s from work-site screenings at Baltimore and East Boston.

Modification of local recruitment plans and clinic operations. Because the number of randomizations after five months of recruitment was lower than expected, each clinic evaluated its recruitment strategy. All clinical centers undertook additional recruitment strategies to widen the net for potentially eligible TOHP participants. Each clinic instituted measures to make participation in TOHP more attractive. Some centers expanded their clinic hours to include early morning, noon, late afternoon, or early evening appointment times to accommodate potential screenees. One TOHP center offered Saturday hours. Other centers set up satellite clinics closer to the suburbs or work sites. Some hired additional staff to accommodate the increase in screening hours.

The number of visits escalated rapidly with the intensification of screening efforts, and many clinics encountered problems handling the increased volume. One clinical center began to use an initial, single BP measurement with a standard manometer to determine eligibility for SV1, rather than tie up staff time to complete the entire SV1 visit on candidates who had extremely low initial BP readings and were unlikely to qualify. Seven of the TOHP centers eventually adopted this initial BP measurement as part of a clinic prescreen to improve efficiency.

The demographic and lifestyle characteristics of all candidates initially screened as compared with those randomized appear in Table 5. Although 44% of the screenees were women, only 30% of those randomized were women. The overall randomization rate for women was 8.9%, compared to 16.2% for men; women had lower eligibility rates than men at each screening visit primarily because the women were more likely to be ineligible because of low BP. The randomized population was 15% black and 82% white; the percentage of blacks was higher in the randomized group than the screened group. Overall, blacks had a higher randomization rate (15.6%) than whites (12.9%), and at each screening visit black candidates were less likely than white candidates to be excluded for low BP. Sixteen percent of those screened were current smokers, compared to 12% of those randomized. In addition, the randomized group included a higher percentage of persons with a four-year college degree than the group of those who were screened.

Table 4. Results of work-site screenings by clinic

Clinic	Number screened	% of total number of initial screening visits	% of total randomized
Baltimore	7,156	69	83
Birmingham	—[a]	17	17
Davis	1,118	2	2
East Boston	3,136	29	34
Jackson	2,334	15	15
Newark	3,462	37	—
Pittsburgh	—	20	20
St. Louis	13,478	84	—

Dash indicates figures are not available.

DISCUSSION

Recruitment of 2,100 participants for Phase I of TOHP was a large and complex task. Not only did enrollees have to meet strict eligibility criteria for DBP (80–89 mm Hg based on the mean of nine readings taken over three visits), but they also had to meet additional common eligibility requirements to allow a

Table 5. Characteristics of the population in TOHP Phase I

Characteristic	Screened		Randomized	
	n	(%)	*n*	(%)
Age (years)				
<30	41	(0.2)	0	(0.0)
30–39	6,079	(36.3)	684	(31.3)
40–49	7,572	(45.3)	1,055	(48.4)
50–54	2,981	(17.8)	443	(20.2)
55–59	38	(0.2)	0	(0.0)
≥60	13	(0.1	0	(0.0)
Sex				
Male	9,429	(56.3)	1,529	(70.1)
Female	7,313	(43.7)	653	(29.9)
Race				
White	13,918	(83.2)	1,793	(82.2)
Hispanic	304	(1.8)	26	(1.2)
Black	2,096	(12.5)	328	(15.0)
Asian	254	(1.5)	26	(1.2)
Other	152	(0.9)	9	(0.4)
Smoking status				
Never smoked	5,526	(53.2)	1,229	(56.4)
Past smoker	3,212	(30.9)	698	(32.0)
Current smoker	1,658	(15.9)	254	(11.6)
Education level				
High school or less	1,965	(18.9)	316	(14.5)
Some college	3,620	(34.8)	719	(33.0)
College degree four-year	1,779	(17.1)	451	(20.7)
Postgraduate	3,029	(29.1)	695	(31.9)

fair comparison of the seven interventions being tested. In spite of the magnitude of this task, a total of 2,182 participants (104% of the goal) were randomized with only a short extension of the planned recruitment period.

The recruitment experience in Phase I of TOHP was comparable to that reported for other similar clinical trials. For example, both the Systolic Hypertension in the Elderly Program and the Hypertension Prevention Trial also relied on mailings as a major recruitment strategy.[4,5] In addition, as in other trials,[4,6–10] the recruitment period for TOHP had to be extended to achieve the intended number of randomized participants. As in three of these other trials,[8–10] the target recruitment goal was eventually exceeded.

Though ultimately successful, the extension of the recruitment phase resulted in an increase in recruitment costs and a slight reduction in the length of follow-up. A major factor in the recruitment problems experienced in TOHP was the underestimation of the overall number of initial contacts necessary to randomize the expected numbers of participants (either generated through direct mailing, community, or work-site screenings). At some clinical centers, the number of BP-eligible candidates was less than anticipated. In general, selling the concept of hypertension prevention to potential candidates was difficult. Although specific information on family history of hypertension was not collected, the concepts of having a "high-normal" BP and, therefore, being at increased risk of developing hypertension appeared to be better received by candidates who had a family member with hypertension.

Prescreening that included BP measurement generally resulted in an increased SV1 eligibility rate and an increased randomization yield. Recruitment staff reported that the personal contact in face-to-face prescreening, rather than telephone prescreening, resulted in better attendance at screening visits.

The recruitment experience in Phase I of TOHP emphasizes the need to have a backup recruitment plan and a system for the early detection of recruitment problems. The three centers that used a cohort recruitment effort were in the best position to recognize problems early. These three centers set definite targets for recruitment of cohorts within specified time frames. If necessary, the efforts for recruitment of subsequent cohorts could be adjusted later to compensate for earlier shortfalls. Recruitment using the cohort approach allowed for more efficient coordination of mailings, work-site screenings, and screening visit schedules. The clinics using the cohort approach randomized 113% to 173% of their goals, whereas clinics using the continuous method reached 27% to 109% of their goals.

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APPENDIX 1

Participating Institutions and Principal Staff

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APPENDIX 2

Exclusion Criteria

1. Evidence of current hypertension, as defined by nine baseline DBP readings averaging 90 mm Hg or greater, or current use (within the previous two months) of antihypertensive medications.
2. Diastolic BP <80 mm Hg, based on the average of nine readings.
3. Gross obesity, BMI ≥ 0.0514 lb/in² (36.14 kg/m²).
4. History of any cardiovascular disease, including myocardial infarction, angina, intermittent claudication, congestive heart failure, and stroke.
5. History of diabetes mellitus, defined by self-report or ever use of insulin or oral hypoglycemic agents.
6. History of chronic renal failure or kidney stones.
7. Recent history of psychiatric disorders, defined by hospitalization within the previous five years for such a condition or current use of antipsychotic or antidepressant medications.
8. History of malignancy (other than nonmelanoma skin cancer) in past five years.
9. History of chronic gastrointestinal disease, such as peptic ulcer, diverticulitis, ulcerative colitis, inflammatory bowel disease, or other conditions judged by study clinician to be a contraindication to admission to TOHP.
10. Serum cholesterol level ≥260 mg/dL.
11. Serum creatinine level ≥1.7 mg/dL for men or 1.5 mg/dL for women.
12. Casual serum glucose ≥200 mg/dL.
13. Other medical history or current treatment that would contraindicate participation in any of the TOHP interventions.
14. Current pregnancy or intent to become pregnant during the study period.
15. Current alcohol intake of more than 21 drinks per week.
16. Inability to cooperate as assessed by clinic staff.

REFERENCES

1. Satterfield S, Cutler JA, Langford HG, et al. Trials of Hypertension Prevention: Phase 1 design. Ann Epidemiol 1991;1:455–71.

2. Cook NR, Rosner B. Screening rules for determining blood pressure status in clinical trials: application to the Trials of Hypertension Prevention. Am J Epidemiol [in press].

3. The Trials of Hypertension Prevention Collaborative Research Group. The effects of nonpharmacologic interventions on blood pressure of persons with high normal levels: results of the Trials of Hypertension Prevention (Phase 1). JAMA 1992;267:1213–20.

4. Petrovich H, Byington R, Bailey G, et al. Systolic Hypertension in the Elderly Program (SHEP). Part 2: screening and recruitment. Hypertension 1991;17(suppl 2):2-16–2-23.

5. Borhani NO, Tonascia J, Schlundt DG, Prineas RJ, Jeffreys JL (for the Hypertension Prevention Trial Research Group). Recruitment in the Hypertension Prevention Trial. Controlled Clin Trials 1989;10:30S–39S.

6. Hunninghake DB, Darby CA, Probstfield JL. Recruitment experience in clinical trials: literature summary and annotated bibliography. Controlled Clin Trials 1987;8:6S–30S.

7. The Lipid Research Clinics Program. Participant recruitment to the coronary primary prevention trial. J Chron Dis 1983;36:451–65.

8. Bradford RH. Participant recruitment to the Lipid Research Clinics Coronary Primary Prevention Trial. Controlled Clin Trials 1987;8:31S–40S.

9. Neaton JD, Grimm RH, Cutler JA (for the MRFIT Research Group). Recruitment of participants for the Multiple Risk Factor Intervention Trial (MRFIT). Controlled Clin Trials 1987;8:41S–53S.

10. Ford CE, Langford HG, Palmer MJ. Recruitment in the Hypertension Detection and Follow-up Program. Controlled Clin Trials 1987;8:54S–67S.