

Getting clinical trial results into practice: design, implementation, and process evaluation of the ALLHAT Dissemination Project

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Background Conventional dissemination of clinical trial results has inconsistent impact on physician practices. A more comprehensive plan to influence determinants of prescribing practices is warranted.

Purpose To report the response from the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial to the National Heart, Lung, and Blood Institute's requirement for dissemination and evaluation of trials with potential immediate public health applicability.

Methods ALLHAT's dissemination plan had two-components: (1) a traditional approach of media coverage, scientific presentation, and publication; and (2) a theory-based approach targeting determinants of clinician behavior. Strategies included: (1) academic detailing, in which physicians approach colleagues regarding blood pressure management, (2) direct patient messages to stimulate communication with physicians regarding blood pressure control, (3) approaches to formulary systems to use educational and economic incentives for evidence-based prescription, and (4) direct professional organization appeals to clinicians.

Results One hundred and forty-seven Investigator Educators reported 1698 presentations to 18,524 clinicians in 41 states and the District of Columbia. The pre- and post-test responses of 1709 clinicians in the face-to-face meetings indicated significant changes in expectations for positive patient outcomes and intention to prescribe diuretics. Information was mailed to 55 individuals representing 20 professional organizations and to eight formulary systems. Direct-to-patient messages were provided to 14 sites that host patient newsletters and Web sites such as health plans and insurance companies, 62 print mass media outlets, and 12 broadcast media sites.

Limitations It was not within the scope of the project to conduct a randomized trial of the impact of the dissemination. However, impact evaluation using quasi-experimental designs is ongoing.

Conclusion A large multi-method dissemination of clinical trial results is feasible. Planning for dissemination efforts, including evaluation research, should be considered as a part of the funding and design of the clinical trial and should begin early in trial planning. *Clinical Trials* 2009; 0: 1–15. <http://ctj.sagepub.com>

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Nomenclature

| | |
|--------|--|
| ACE | Angiotensin-converting enzyme |
| ALLHAT | Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial |
| BP | Blood pressure |
| CCB | Calcium channel blocker |
| CDC | Centers for Disease Control and Prevention |
| CME | Continuing medical education |
| CVD | Cardiovascular disease |
| DASH | Dietary Approaches to Stop Hypertension |
| HF | Heart failure |
| IE | Investigator Educator |
| IM | Intervention mapping |
| IRB | Institutional review board |
| JNC7 | Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure |
| MSA | Metropolitan statistical area |
| NHBPEP | National High Blood Pressure Education Program |
| NHLBI | National Heart, Lung, and Blood Institute |
| NIH | National Institutes of Health |
| VA | Department of Veterans Affairs |

Background

Translational science includes both an interface between basic science (bench) and clinical medicine (bedside) and one between clinical medicine and ensuring that treatments based on evidence actually reach the appropriate patients and have an impact on the public's health (community) [1]. Results of clinical trials that objectively evaluate the safety and efficacy of medications and other interventions are the cornerstone of evidence-based practice. However, the impact on medical practice of these clinical trials may be less than optimal [2,3]. This issue may be particularly important for older interventions that lack corporate promotion, but are shown to be the best choices for therapy. Traditional dissemination of clinical trial results, especially presentation at scientific conferences and publication in scientific journals, may be inadequate to stimulate practice changes [1–14].

One effort to disseminate antihypertensive trial results was the National High Blood Pressure Education Program (NHBPEP) of the National Heart, Lung, and Blood Institute (NHLBI). In 1971, the NHLBI organized this consortium of 47

professional and voluntary associations to create and maintain an education program to disseminate results from major multicenter clinical trials of antihypertensive treatment conducted since the 1960s, several with Federal sponsorship [15–18]. The NHBPEP influenced the relatively steady progress in awareness, treatment, and control of hypertension and likely contributed to the dramatic decline in mortality from cardiovascular diseases (CVDs) [19,20]. Nevertheless, progress in translating clinical research advances into practice has fallen short of Healthy People 2000 [21] blood pressure (BP) goals. The NHLBI leadership had increasingly attempted to stimulate and direct innovative methods to accelerate this kind of translation, especially in the period immediately following additional major trials [22–24] and funded research in this area [25,26].

A recent clinical trial with major implications for public health was the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). ALLHAT was a randomized, double-blind, practice-based, multicenter clinical trial designed to determine whether the occurrence of fatal coronary heart disease or nonfatal myocardial infarction is lower for high-risk hypertensive patients treated with a calcium channel blocker (represented by amlodipine), an angiotensin converting enzyme (ACE) inhibitor (represented by lisinopril), or an alpha blocker (represented by doxazosin), each compared with a diuretic (represented by chlorthalidone) [27]. Secondary endpoints included stroke, heart failure (HF), all-cause mortality, and renal disease. To evaluate differences in effects of the four treatments on cardiovascular and renal outcomes, ALLHAT was designed with a large sample size (40,000 participants) and long follow-up (up to 8 years). The doxazosin arm was discontinued in February 2000 in light of a significantly increased occurrence of CVD, especially HF, and because of futility for finding a difference in the primary endpoint (part of the a priori stopping guidelines for ALLHAT) when compared with the chlorthalidone arm [28]. The final results for the other two comparisons, reported in December 2002 [29], showed no differences for the primary endpoint or all-cause mortality. However, the trial showed that first-step treatment based on an inexpensive thiazide-type diuretic was superior to treatment based on other widely prescribed drug classes in preventing one or more major forms of CVD, and recommended that, thiazide-type diuretics should be preferred for first-step antihypertensive drug therapy [29,30].

After the publication of ALLHAT results, there was some increase in prescriptions of thiazide-type diuretics at hypertension visits. However, the lack of a continued increase in thiazide prescriptions

over the next year provided further evidence of the need for a more active dissemination plan, as had been discussed by investigators at the time of the publication of the ALLHAT main results [31,32].

The purpose of this report is to describe the development, implementation, and process (implementation) evaluation of a multifaceted, theory-informed intervention to disseminate the results of the ALLHAT trial and the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC 7) guidelines beyond the standard publication and presentation of trial results. In addition to this design paper, the longer-term dissemination of ALLHAT was evaluated in two studies, one analyzing national prescription trends and another in the context of dissemination of hypertension guidelines in the Department of Veterans Affairs (VA).

Methods

Intervention development

Planning framework and core dissemination messages

We used the Intervention Mapping (IM) [33,34] framework to plan the ALLHAT/JNC 7 Dissemination Project, 'Improving Blood Pressure Treatment in the Community: A Joint Project of the National High Blood Pressure Education Program (NHBPEP) and ALLHAT Collaborative Research Group'. IM, a systematic process for health promotion program planning, has been used to guide development of numerous programs, several of which included change strategies for health care providers [35–37].

We began by identifying health care providers who manage hypertension as the priority population for practice behavior change and set an objective of reaching approximately 30,000 health care providers in the United States. This is about 15% of the approximately 180,000 practicing internists and family practitioners in the United States [38]. According to Berwick (2003) [39,40], the tipping point for dissemination to occur is for 15–20% of a group to adopt the innovation. Although the priority population for behavior change was the health care providers, we also targeted change in their environment, and the intervention was implemented both directly to providers and indirectly through messages to patients.

Dissemination messages

The main dissemination messages articulated the treatment goals and expectations for hypertensive

patients and were based on both the results of ALLHAT and the recommendations of the JNC 7 report. The messages were reviewed and endorsed by the NHBPEP to acquire broad-based consensus from among organizations that represent health care providers who treat hypertension [41]. They were the following:

- (1) The BP goal for most patients with hypertension is <140/90 mm Hg.
- (2) Most patients diagnosed with hypertension should experience better BP control after adopting lifestyle modifications.
- (3) Most patients diagnosed with stage 1 hypertension (systolic BP [SBP] 140–159 or diastolic BP [DBP] 90–99 mm Hg) should experience better BP control and better long-term CVD risk while taking a thiazide-type diuretic.
- (4) Most patients with stage 2 hypertension (SBP \geq 160 or DBP \geq 100 mm Hg) should experience better BP control and better long-term CVD risk when taking a multidrug regimen that includes a thiazide-type diuretic.
- (5) Most patients with uncontrolled hypertension should experience better BP control and better long-term CVD risk when a thiazide-type diuretic is added to the patient's treatment regimen.

Although these were the agreed upon treatment recommendations, the messages were elaborated by combining the desired behavior goals with factors that influence health care provider behavior.

Theoretical framework and elaboration of core messages

Working from a social cognitive theory (SCT) framework [39,40], we developed planning matrices (Tables 1 and 2) that combined detailed descriptions of the targeted health care provider behavioral change as well as expectations for communication by patients and other aspects of the providers' environments. We then worked from the matrices to develop plans for program delivery. We chose SCT because it focuses on both individual cognitive influences on behavior and on social environmental influences. SCT provides a framework that incorporates categories of barriers and facilitators of the adoption of evidence-based practice changes [42,43]. For example, Cabana and colleagues describe approximately 50 barriers and facilitators in categories of knowledge, attitudes, external barriers, guideline factors, and environmental factors. SCT explicates similar categories of factors including cognitive and affective factors

Table 1 Intervention planning matrix for provider behavior

| Performance objectives | Awareness and behavioral capability | Skills and self-efficacy | Outcome expectations | Pharmaceutical marketing influence | Perception of social norms and standards of care |
|---|--|--|--|---|---|
| 1. Prescribe diuretic as first treatment (Stage 1 HTN) | <ul style="list-style-type: none"> Recognize the JNC 7 guideline to start with a diuretic for SBP 140–159 or DBP 90–99 mmHg Describe the results and conclusions of the ALLHAT study Recognize that patients with compelling indications need other or multiple drugs Describe ALLHAT as the largest head-to-head comparison relevant to Stage 1 HTN Recognize that normal blood pressure is <120 and <80 mm Hg | <ul style="list-style-type: none"> Express confidence in prescribing according to JNC 7 guidelines | <ul style="list-style-type: none"> Expect that patients will have better BP control when treated with diuretic Expect better long-term CVD risk, especially for heart failure, with diuretic treatment Expect simplified first-line treatment decisions when consistently prescribing diuretics Expect better adherence related to cost when prescribing diuretics | <ul style="list-style-type: none"> Compare diuretics to other drugs regarding CVD outcomes and price Recognize messages that lobby against diuretics without scientific basis Reflect critically on origin of personal HTN drug preferences and biases | <ul style="list-style-type: none"> Forecast that many other clinicians prescribe diuretics as first treatment Describe JNC 7 as recommending diuretics as standard of practice for first treatment of Stage 1 HTN Expect that the monitoring required with diuretic is worked into practice routines by other physicians |
| 2. Prescribe a two-drug combination for Stage 2 HTN (Stage 2 HTN) | <ul style="list-style-type: none"> Discuss JNC 7 guidelines, ALLHAT conclusions, and dosing for a two-drug combination usually including diuretic for patients with SBP \geq 160 or DBP \geq 100 mmHg Recognize that patients with compelling indications need other or multiple drugs | <ul style="list-style-type: none"> Express confidence in prescribing for stage 2 hypertension according to the JNC 7 guidelines | <ul style="list-style-type: none"> Expect that prescribing diuretics will enable stage 2 HTN patients to have better BP control Expect that prescribing a diuretic will enable stage 2 HTN patients to have better long-term CVD risk | <ul style="list-style-type: none"> Describe proportion of patient income represented by each regimen | <ul style="list-style-type: none"> Recognize that other clinicians routinely prescribe two-drug combinations for stage 2 hypertension |
| 3. If a patient is treated and uncontrolled, add a diuretic to the medication regimen | <ul style="list-style-type: none"> Describe ALLHAT conclusions, JNC 7 guidelines, and dosing related to adding medications Describe that JNC 7 and ALLHAT suggest a diuretic as part of any multidrug regimen | <ul style="list-style-type: none"> Express confidence in adding diuretic to a regimen of uncontrolled patients | <ul style="list-style-type: none"> Expect better BP control and long-term CVD health by adding a diuretic when a patient is treated and uncontrolled | <ul style="list-style-type: none"> Recognize that free samples are only a short term help | <ul style="list-style-type: none"> Recognize that other clinicians are adding a diuretic to an uncontrolled patients regimen |

| | | | | |
|--|---|--|--|---|
| <p>4. Discuss with patient the benefits and side-effects of diuretics</p> | <ul style="list-style-type: none"> Describe goals and expectations of better blood pressure control and better long-term CVD health Describe side-effects as manageable | <ul style="list-style-type: none"> Express confidence in medication adherence counseling | <ul style="list-style-type: none"> Expect that patient will appreciate discussion of BP control, long-term CVD health, and cost of drugs Expect that discussion will improve adherence | <ul style="list-style-type: none"> Recognize that other providers discuss BP control and diuretics with patients |
| <p>5. Recommend that hypertensive patient undergo lifestyle modification</p> | <ul style="list-style-type: none"> Describe contributions of weight reduction, physical activity, moderate consumption of alcohol, and following the DASH eating plan to HTN control | <ul style="list-style-type: none"> Express confidence in ability to deliver motivational messages | <ul style="list-style-type: none"> Expect that brief clinician counseling can help patients commit to behavioral change | <ul style="list-style-type: none"> Recognize that other respected clinicians are recommending lifestyle modification |

such as awareness of or familiarity with guidelines, behavioral capability and skills (knowing what to do and how to do it), self-efficacy, and outcome expectations for practice change. Social influences include patient behaviors such as adherence and follow-up for reevaluation, commercial marketing, and presence of guidelines and standards of care. Barriers to practice change may also include the lack of opportunity for reinforcement, which most naturally should come from improvements in patient BP control, but may be lacking when patients are nonadherent, are not consistently followed, or the clinician lacks skills or resources to treat resistant hypertension.

We developed matrices for both the priority population (providers) (Table 1) and the agents in the environment who provide the external influences on health care provider behavior (Table 2). The tables explain what health care providers should do (behavioral performance objectives in the left column) and hypothesized barriers and facilitators including external influences such as pharmaceutical company marketing (column heads). The cells of the matrices comprise change objectives, the immediate targets of the behavior change intervention, and the basis of the elaborated messages.

Intervention plan

A theory-based intervention method is a defined process by which theory postulates how behavior change may occur in an individual, a small group, or other social structure, whereas a strategy is a way of organizing and delivering the intervention methods [33]. An example of a theory-based method is modeling [39], which is frequently used to facilitate behavior change. In this step, we proposed a multilevel intervention to deliver change methods and practical strategies intended to influence the objectives in each matrix. The strategies involved direct and indirect approaches. The direct approach intended to influence physicians through academic detailing and their professional societies. The indirect approach intended to influence physicians through their patients and drug formulary systems.

The investigator educator (IE) approach was the primary strategy to achieve the objectives in the Table 1 matrix. It is based on academic detailing [44,45]. The plan was to reach providers using 180 IEs – mostly physicians who had participated in the ALLHAT trial as clinical investigators. Regional coordinators with clinical trial experience, including at least several years in ALLHAT, interviewed prospective educators to discuss their typical professional networks and the potential to reach providers

Table 2 Environmental matrix formulary and patient behavior change

| Performance objectives | Awareness, behavioral capability | Skills and self-efficacy | Outcome expectations | Pharmaceutical marketing Influence | Perception of social norms and standards of care |
|---|--|---|--|---|---|
| pharmacy managers | | | | | |
| 1. Benefits managers implement formulary parameters to provide cues for diuretic use as first-line HTN medication | <ul style="list-style-type: none"> Recognize that JNC 7 recommends starting with diuretic and diuretic as part of multdrug regimen Describe ALLHAT results and conclusions Describe dosing recommendation | | <ul style="list-style-type: none"> Expect that patients will have better BP control and better long-term CVD risk profile when treated with diuretics Expect cost savings to the pharmacy plan | <ul style="list-style-type: none"> Compare diuretics to other drugs regarding CVD outcomes and price Recognize messages that lobby against diuretics without scientific basis Reflect critically on origin of personal HTN drug preferences and biases | <ul style="list-style-type: none"> Recognize that other formularies are changing to control HTN treatment costs and to achieve better outcomes |
| patients | | | | | |
| 1. Newly diagnosed patients and those with uncontrolled hypertension will ask providers about diuretics | <ul style="list-style-type: none"> Describe guidelines for diuretics as first-step therapy and addition to regimen if uncontrolled Recognize that new recommendations suggest diuretics as first-step therapy and as addition to regimen if uncontrolled Describe diuretics as having some adverse impact on blood sugar; nevertheless, positive study results held for diabetics | <ul style="list-style-type: none"> Express confidence in asking about diuretic Express confidence in asking if a medication change is indicated | <ul style="list-style-type: none"> Expect providers to respond positively to communication about BP control and diuretics Expect communicating with provider about diuretic will result in better BP control and long-term CVD health Expect adding a diuretic may result in less need for expensive multidrug regimens | <ul style="list-style-type: none"> Recognize that guidelines suggest continuing to work on BP control until goals are met Describe friends and relatives as talking to the doctor about treatment for blood pressure | |
| 2. Patients with diagnosed hypertension will engage in conversation about lifestyle modification with physician | <ul style="list-style-type: none"> Recognize that JNC 7 and ALLHAT results recommend that lifestyle modifications should be treatment for HTN Describe importance of weight reduction, physical activity, moderate consumption of alcohol, and following the DASH eating plan | <ul style="list-style-type: none"> Express confidence in making lifestyle changes | <ul style="list-style-type: none"> Expect that working with the physician can help with commitment to behavioral change Expect that physical activity and approaching normal weight will result in better BP control and better long-term CVD risk Expect that even modest changes can make a difference in BP | <ul style="list-style-type: none"> Recognize that valued love ones, friends, and colleagues think that making changes in weight and exercise is very important | |

beyond these routine contacts. They also considered the ability of the investigator to recruit patients during the clinical trial, their success in retention and adherence during the trial, and their potential as persuasive behavior change educators. The project team attempted to recruit educators broadly from all regions of the United States.

The change methods to be delivered through this personal contact strategy were: (1) persuasion by presenting two-sided arguments and eliciting reservations of participants, (2) role modeling from a respected peer or opinion leader, and (3) provision of information and cues to action through materials given to providers at presentations. IEs were trained in day-long face-to-face workshops to present the JNC 7 as the framework for BP control, describe the results of the ALLHAT trial, make the results relevant to personal practice, model the use of the guidelines and results, actively encourage use, and stimulate questions and discussion. In the training, the educators were also asked to begin to plan potential venues for these presentations and discussions. The goal for the educators was for each one to make 12 presentations to small groups over 12 months and reach an estimated 156 providers (per IE) who prescribe drugs for hypertension. They were asked to make a special effort to reach opinion leaders, clinicians who influence the opinions of colleagues in their geographic areas. We explained that opinion leaders are physicians who are respected in the local community, trusted by their peers, and likely to be persuasive role models for colleagues regarding clinical practice; however, we did not provide a systematic process for the IEs to use to identify opinion leaders such as a survey or network analysis [46]. The proposed settings were medical practice staff meetings, hospital staff meetings, residency programs, local medical societies, and other venues as identified by the educator, regional coordinator, or central project coordinator. IEs were compensated with \$400 per presentation to cover purchase of a light meal or snack for the participants at the session, travel to the venue, and an honorarium. Prior to full implementation, we conducted a pilot phase with 24 IEs for 6 months to test feasibility of the approach.

The IEs were to leave cues to action with participants including a newsletter with examples of changes in BP treatment (role model stories), pocket cards summarizing main BP control messages and skills for encouraging lifestyle changes, JNC 7 reference cards, the JNC 7 Express report [47], reprints of two ALLHAT publications, tips for accurate BP measurement, and a copy of the Dietary Approaches to Stop Hypertension (DASH) diet. Participants were

also offered exam room posters to encourage patients to talk with their doctors and a small 'prescription pad' to record recommendations for patient BP goals and plans for lifestyle changes.

The regional coordinators contacted educators periodically to assess progress, encourage contacts, and help with finding venues. The ALLHAT Clinical Trials Center provided training, materials, and support for the coordinators and for the IEs. Brief reports on each completed venue were collected, data entered, and analyzed to provide ongoing process evaluation for this component of the dissemination effort.

A secondary strategy for reaching health care providers was through their professional associations. We solicited participation from 20 associations selected from members of the NHBPEP coordinating committee with a letter tailored to the focus of the association. We asked them to communicate project messages to their membership and we provided a sample letter, a model article for the association newsletter, and reprints of the primary ALLHAT publications.

The interventions related to Table 2 were indirect influences on physician behavior. We sought to stimulate the 10 pharmacy benefit systems that managed approximately 80% of prescription-covered lives to initiate education and incentives for prescribing according to JNC 7 guidelines. We provided formulary managers with letters including the project core messages, a summary of key ALLHAT results and JNC 7 recommendations, a statement of the importance of the ALLHAT results to formulary management, cost information, and ALLHAT articles.

We also provided press kits to IEs to use with community media and encouraged the issuance of an NHLBI press release to stimulate community interest in the dissemination project and to highlight the commitment of local physicians to evidence-based treatment of hypertension. In addition, we contacted both print and broadcast media outlets to assess their interest in running items on the project and to provide sample stories.

Process evaluation measures

We designed a protocol for process evaluation to assess the 'reach' and 'dose' of the implementation of the dissemination interventions. The University of Texas Institutional Review Board (IRB) reviewed and approved the protocol under the exempt category. Reach is the proportion of the intended priority population who participated in the

Table 3 Investigator educator reach and dose delivered by region

| Region | Number of presentations | Total number of clinician participants | Average number of clinician participants per presentation | Population age 50+ years ^a | Clinician participants per 10,000 population 50+ years |
|-----------|-------------------------|--|---|---------------------------------------|--|
| Total | 1698 | 18,524 | 10.9 Range 1.0–106.8 | 76,381,962 | 2.43 Range 0.01–86.11 |
| Midwest | 542 | 4388 | 8.1 Range 1.0–56.0 | 17,813,111 | 2.48 Range 0.01–86.11 |
| Northeast | 341 | 3274 | 9.6 Range 1.4–72.0 | 15,661,538 | 2.09 Range 0.20–9.50 |
| South | 655 | 7898 | 12.1 Range 1.0–106.8 | 27,530,500 | 2.87 Range 0.01–41.69 |
| West | 160 | 2964 | 18.5 Range 1.0–32.0 | 15,376,813 | 1.93 Range 0.05–18.39 |

^aFrom <http://datawarehouse.hrsa.gov/pcsa.htm>, files MSA1.DBF and COUNTY1.DBF, accessed July 16, 2007.

intervention [48]. We defined reach as the number of health care providers (clinicians) who attended face-to-face sessions with IEs. Based on IEs completing questionnaires, we recorded the number of IEs, the number of presentations, and characteristics of the presentations including geographic location and audience size. For each IE reporting over 15 venues as of October 2006 (eight IEs), we selected 20% of the reports to validate by calling participants or venue staff. These counts included both the pilot and full-scale phases of the strategy.

Another assessment was the dose. The 'dose delivered' was the amount of intervention that was delivered or provided to the intended audience [49]. For dose-delivered calculations, the denominator was the population over 50 years of age in the metropolitan statistical areas (MSA) where the presentations occurred. We calculated the median ratio for IE presentations per MSA 10,000 population over 50 years. We also reported mean number of clinician-attendees per MSA 10,000 population over 50 years.

We assessed response of attending clinicians with pre-post measurement. Because we had targeted behavior change rather than strictly knowledge, we measured cognitive factors that may be related to behavior (influenced by knowledge) including intentions, self-efficacy, and expectations of benefit from changing prescribing practices to be more congruent with the program messages. These pre-post questionnaires were distributed at the IEs' discretion, which was dependent on the time allotted for the presentation, arrangements with the venue, and whether they had IRB approval.

For the interventions targeted at patients, professional associations, and formulary managers, the quantitative process assessments for reach and dose were beyond the scope of the dissemination

program except for descriptive statistics of the number of contacts made to formulary managers, print and broadcast media, and professional associations.

Results

Reach and dose

IE presentations are enumerated by regions in Table 3. The regional means are calculated from presentations in each MSA in the region. (Table 3 detail by MSA is available from the corresponding author.) The 147 educators (the number recruited from the goal of 180) reported a total of 1698 presentations to more than 18,500 participants in combined pilot and full implementation in 41 states and the District of Columbia between September 2004 and March 2007. Average attendance was 10.9. The median ratio of presentations to MSA population was 2.43 per 10,000 populations over 50 years of age (a denominator of older adults at increased risk of hypertension). The validation involved attempts to contact participants or staff at 29 of the venues for 8 IEs; 21 were successfully contacted, and 19 presentations were verified (90%).

We mailed information to 55 individuals representing 20 professional organizations and to eight formulary systems that covered more than 80% of US prescriptions as of July 2005. Follow up mailings and phone calls were made to 34 individuals.

For the indirect approach to health care providers through patients, we contacted 14 sites that host patient newsletters and Web sites such as health plans and insurance companies, 62 print mass media outlets, and 12 broadcast media sites.

Table 4 Attitude and intention scores pre- and post-IE presentations^a

| | Total | 1, do not agree at all; 5 - Agree completely | | | | | Mean (SD) ^b |
|---|-------|--|-------------|-------------|-------------|--------------|------------------------|
| | | 1 | 2 | 3 | 4 | 5 | |
| Outcome expectations | | | | | | | |
| <i>I expect that my patients will have better BP control when treated with diuretic</i> | | | | | | | |
| Pretest | 1709 | 18 (1.1%) | 61 (3.6%) | 275 (16.1%) | 692 (40.5%) | 663 (38.8%) | 4.12 (0.88) |
| Posttest | 1617 | 5 (0.3%) | 8 (0.5%) | 80 (4.9%) | 499 (30.9%) | 1025 (63.4%) | 4.57 (0.64) |
| <i>I expect better long-term CVD risk among diuretic-treated hypertensive patients</i> | | | | | | | |
| Pretest | 1681 | 41 (2.4%) | 108 (6.4%) | 372 (22.1%) | 669 (39.8%) | 491 (29.2%) | 3.87 (0.99) |
| Posttest | 1595 | 36 (2.3%) | 41 (2.6%) | 113 (7.1%) | 535 (33.5%) | 870 (54.5%) | 4.36 (0.89) |
| Attitude toward ALLHAT | | | | | | | |
| <i>I believe the HF results from the ALLHAT clinical trial</i> | | | | | | | |
| Pretest | 1540 | 79 (5.1%) | 191 (12.4%) | 733 (47.6%) | 320 (20.8%) | 217 (14.1%) | 3.26 (1.02) |
| Posttest | 1535 | 144 (9.4%) | 198 (12.9%) | 379 (24.7%) | 412 (26.8%) | 402 (26.2%) | 3.48 (1.27) |
| <i>I anticipate good acceptance of diuretic treatment by patients</i> | | | | | | | |
| Pretest | 1688 | 28 (1.7%) | 128 (7.6%) | 421 (24.9%) | 727 (43.1%) | 384 (22.7%) | 3.78 (0.94) |
| Posttest | 1572 | 18 (1.1%) | 36 (2.3%) | 206 (13.1%) | 695 (44.2%) | 617 (39.2%) | 4.18 (0.83) |
| <i>I think diuretics can safely be used for diabetic patients</i> | | | | | | | |
| Pretest | 1674 | 76 (4.5%) | 139 (8.3%) | 365 (21.8%) | 447 (26.7%) | 647 (38.6%) | 3.87 (1.15) |
| Posttest | 1596 | 133 (8.3%) | 135 (8.5%) | 148 (9.3%) | 371 (23.2%) | 809 (50.7%) | 3.99 (1.30) |
| Social norms | | | | | | | |
| <i>I think my colleagues are making changes in their practices regarding blood pressure management</i> | | | | | | | |
| Pretest | 1654 | 58 (3.5%) | 114 (6.9%) | 612 (37.0%) | 585 (35.4%) | 285 (17.2%) | 3.56 (0.97) |
| Posttest | 1576 | 25 (1.6%) | 75 (4.8%) | 423 (26.8%) | 584 (37.1%) | 469 (29.8%) | 3.89 (0.94) |
| Intentions | | | | | | | |
| <i>I expect to retrain my staff in proper blood pressure measurement techniques</i> | | | | | | | |
| Pretest | 1647 | 129 (7.8%) | 140 (8.5%) | 435 (26.4%) | 432 (26.2%) | 511 (31.0%) | 3.64 (1.22) |
| Posttest | 1519 | 88 (5.8%) | 82 (5.4%) | 252 (16.6%) | 422 (27.8%) | 675 (44.4%) | 4.00 (1.16) |
| <i>I anticipate beginning more newly diagnosed hypertensive patients on a diuretic as first-line treatment</i> | | | | | | | |
| Pretest | 1673 | 72 (4.3%) | 101 (6.0%) | 334 (20.0%) | 579 (34.6%) | 587 (35.1%) | 3.90 (1.08) |
| Posttest | 1599 | 39 (2.4%) | 36 (2.3%) | 141 (8.8%) | 468 (29.3%) | 915 (57.2%) | 4.37 (0.91) |
| <i>I add a diuretic, or plan to begin adding a diuretic, to the regimens of uncontrolled patients</i> | | | | | | | |
| Pretest | 1678 | 30 (1.8%) | 50 (3.0%) | 234 (13.9%) | 677 (40.3%) | 687 (40.9%) | 4.16 (0.90) |
| Posttest | 1574 | 41 (2.6%) | 23 (1.5%) | 99 (6.3%) | 450 (28.6%) | 961 (61.1%) | 4.44 (0.88) |
| <i>I anticipate providing lifestyle change counseling more often than is my current practice with hypertensive patients</i> | | | | | | | |
| Pretest | 1686 | 86 (5.1%) | 99 (5.9%) | 370 (21.9%) | 570 (33.8%) | 561 (33.3%) | 3.84 (1.11) |
| Posttest | 1577 | 55 (3.5%) | 55 (3.5%) | 219 (13.9%) | 489 (31.0%) | 759 (48.1%) | 4.17 (1.02) |

^a18,524 attendees, 2667 pretests (14.4% of attendees), 2640 posttests (14.3% of attendees). Range of valid pretest responses is 8.3% to 9.2% of attendees. Range of valid posttest responses is 8.2% to 8.7% of attendees. ^bt-tests comparing mean pretests and mean posttests are all significant at $p \leq 0.005$.

In addition, an NHLBI press release highlighting the dissemination program and the importance of diuretic prescription was sent to the extensive NHLBI media list.

Participant response

Questionnaires were completed by a convenience sample of 1709 respondents for the pretest and 1617 respondents for the posttest. The response of the participants in the face-to-face meetings was positive. As shown in Table 4, the participants demonstrated statistically significant differences in mean scores between pretest and posttest including their expectations for positive patient outcomes and their intention to prescribe diuretics.

Discussion

Practice change – what works?

Studies have yielded divergent results on how much and how rapidly clinical trial results have exerted a significant impact on physician prescribing. For example, changes in postmyocardial infarction treatment [13,50] and warfarin use in atrial fibrillation [51] have been attributed to publication of multiple clinical trials and have taken many years to be incorporated into clinical practice. In contrast, increases in statin prescribing preceded the publication of clinical trials, mostly sponsored by the industry, that demonstrated the specific benefit of statins on hard outcomes, and

these trials had little effect on preexisting trends [52]. In an early study, Fineberg reviewed 28 studies on the effects of specific clinical trials on 19 practices and found only 2 instances where the clinical trial clearly influenced practice [53] and Kudesia and Chaturvedi [54] found little practical impact of negative clinical trials regarding intravenous heparin use in acute ischemic stroke. Moreover, a lack of influence of a randomized clinical trial even on its participating investigators has been suggested [55,56]. As mentioned above, the publication of the results of ALLHAT, shortly followed by the JNC 7 hypertension guidelines, were associated with a substantial initial increase in diuretic prescriptions, but the change apparently leveled out quickly [31], suggesting the need for intervention beyond the publication of trial results and their incorporation into newly published guidelines. A recent study showed some sustained increase in diuretic use in a large managed care organization but suggested continuing opportunity to increase adherence to the JNC 7 [57].

Intervention beyond the publication of trial results often has been limited to standard continuing medical education (CME), which has been recently described in two systematic reviews as having some impact on practice behavior [58,59]. However, effect sizes were small to moderate, and the quality of intervention descriptions did not allow differentiations to be made between types of education except that interactive sessions are better than didactic sessions alone [58] and live media was more effective than print, multimedia more effective than single media, and repeated exposure more effective than single exposure [59]. Other authors recommend that interventions should be more intensive than CME and suggest multilevel interventions (combinations of knowledge and skill enhancement, attitude change, behavioral feedback, patient specific guidance, and cues or reminders) may be necessary to improve physician and patient adherence to guidelines and best medical practice [14,45,60–65]. To promote clinician adoption of recommended practices, efforts in addition to scientific publication should take into account a range of influences such as patient preferences, drug promotion, recommendations from clinical colleagues and guidelines, and features of particular pharmaceuticals, including their price and generic status, on clinician adoption of recommended practices [6–10]. Interventions using multiple methods including audit and feedback, detailing by local opinion leaders, patient components and community- and practice-based methods to target this range of influences have shown greater effectiveness than traditional CME [4,10–14].

In addition, a number of researchers have called attention to the need for theory- and evidence-

based interventions [11,66,67]. For example, Davis and Taylor-Vaisey [11] have focused on evidence for multiple levels of causation in provider adoption of practice guidelines and have suggested that interventions focus on behavior through influencing factors at the provider, patient, practice, profession, and sociopolitical levels.

The intervention described in this report consisted primarily of persuasive communication regarding change in prescribing practices presented by colleagues in the community. We reached 18,524 care providers with face-to-face persuasive messages. Our goal was to focus on behavior change rather than focusing exclusively on improving physician knowledge. The IE strategy had characteristics of effective academic detailing including role modeling by peers, visits to individuals or practice groups, and careful delineation of the target behavior [11,61]. The interactive sessions were based on SCT and sought to influence behavioral capability and skills, attitudes toward ALLHAT and diuretic use, outcome expectations about drug effects and patient acceptance, self-efficacy for prescribing and cues, and reinforcement from patients and formularies in addition to improving knowledge. The intervention was designed to be more intensive than usual CME, but, it did not include individualized efforts such as initiation of practice- or network-based performance standards or audit and behavioral feedback strategies [68–70]. These more individualized strategies may be more powerful in producing behavior change but their implementation would have required individualized approaches to practices and practice systems, thus sacrificing the national reach of this project due to limited resources.

The intervention was intended to be multifaceted and multilevel by stimulating communications to providers through professional societies, formularies, and patients. However, we have little evidence that the intended communications occurred. Some media outlets, professional associations, and formulary managers responded to their constituencies regarding BP control closer to the time of the JNC 7 and ALLHAT results release.

The intervention through formularies may have encountered additional barriers that were not measured in this study. When the ALLHAT Dissemination Project started, generic thiazide-type diuretics were already available as preferred antihypertensive drugs on most formularies. There was little opportunity for an intervention to increase the presence of diuretics on formularies. In addition to formularies, pharmacy benefit managers may use step-therapy programs to influence physician prescribing behavior. Step-therapy programs that were compatible with JNC 7 guidelines were extant before the onset of the ALLHAT Dissemination Project [71].

Pharmacy benefit managers may also influence prescribing behavior indirectly through drug copayments charged to patients to change demand for and adherence to drugs [72,73]. When the dissemination project started, generic thiazide-type diuretics were already available to patients at the lowest tier for copayment. The ALLHAT Dissemination Project did not have the capacity to change copayment or step-therapy programs because they are governed by contracts between the pharmacy benefits managers and their clients who are employers, insurers, managed care organizations, and government agencies.

Limitations

The cost of the dissemination project, including the evaluation studies, was \$3.7 million, approximately 4% of the trial budget and a modest expenditure in the context of the annual cost of hypertension, estimated to have been \$66.7 billion in 2007 [74,75]. It was conceived as an educational effort with an evaluation component rather than a research study. The evaluation plan included the implementation process questions reported in this study. It was not within the scope of this implementation project to conduct a trial of the impact and outcomes of the dissemination. The assessment of change in physician intentions, expectations, and self-efficacy was conducted only on a convenience sample. No generalization to the full group of physicians reached can be made. However, we are conducting a comparison study of national prescribing trends between MSAs with varying intensities of dissemination activities and a report of a similar comparative study in the VA system (in preparation). The project would have been very resource intensive to carry out as a controlled trial on a wide scale, and trade-offs were made in evaluation rigor to achieve wide reach. Trial planners might consider both broad dissemination efforts and smaller dissemination substudies planned prior to the publication of trial results.

Although the dissemination intervention targeted behavior and the barriers and facilitators of practice change, the project did not conduct a barrier assessment prior to developing the intervention; instead, it relied on literature review and a theoretical framework to delineate barriers and facilitators to practice change. Furthermore, methods delivered did not include systems change or attempts to provide clinicians with practice data (audit and feedback). These strategies might have been indirectly included, had we prepared the IEs to teach how to implement audit and feedback and organizational change in the practices reached. However, we conceived of these approaches to require a more hands on, individualized,

resource-intensive interaction with providers and their practices and considered our intended reach and available budget to prohibit these strategies.

The intervention also did not include a sustainability component. Although the evidence is conflicting, practice change of the type targeted in this effort can be self-sustaining based on reinforcement from patient response and BP control. For example, in acute stroke treatment, rates of therapy continued to increase after the intervention [39]. However, we acknowledge that acute stroke treatment change might be different than sustaining behavior change that is frequently challenged by outside influence such as drug marketing.

Lessons learned

Outside influences

The media can have a limited to dramatic effect on how the results of a study become known and interpreted. Articles about ALLHAT appeared in many major newspapers initially and less frequently as time progressed. The ALLHAT leadership made efforts to ensure that the study's findings and our dissemination efforts were presented fairly.

It is possible that limited dissemination efforts on the part of clinical trials cannot offset the vested interest and resources pharmaceutical companies bring to bear on the interpretation of a trial [76]. While the ALLHAT leadership was aware of the efforts of pharmaceutical companies to interpret the ALLHAT results in ways favorable to their products, it was not our intention to respond to or challenge marketing material counter to ALLHAT's message at every turn. However, we first countered these efforts in scientific forums [77,78] and by participating in presentations and debates at scientific conferences such as the American Society of Hypertension and the American Heart Association. Later dissemination efforts countered the efforts more directly within our academic detailing program albeit with comparatively limited resources.

Dissemination partners

Another lesson learned regards considerations of the 'who' in dissemination planning. Who might be available, effective, and willing, at both the individual and organizational levels, to diffuse trial results? Glasgow *et al.* [48] suggest the need for dissemination planning early in the planning of the original trial so that partners who could participate in the dissemination have a stake in the trial

from the beginning. These partners might be different from the clinical and other researchers who are necessary for the conduct of the research. In ALLHAT, there was consideration of dissemination later in the trial, which is a typical scenario. However, it might be questioned whether funders would be willing to invest in this early development of dissemination partners and strategies when trial results are unknown.

Initial dissemination training activities occurred at the final investigator's meeting of the trial and focused on scientific presentation and media approaches rather than behavior change. In addition, the NHBPEP was in place at the NHLBI, and its staff and principal advisors worked with the dissemination project to develop the core messages. When it became clear that further dissemination efforts might be needed to maximize the public health benefit of ALLHAT, the project was fortunate to have a large national network of trial investigators who could be recruited for dissemination activities. However, the question should be asked whether the network was the optimal one for dissemination. IEs in this dissemination had some problems seeking venues. Many were uncomfortable seeking invitations to make a persuasive presentation; they were used to being approached to speak rather than asking for invitations. The trial network members may not have had optimal professional reach or comfort with the tasks of dissemination.

Possible alternative networks might have included large professional associations that are routinely involved in disseminating practice information and guidelines. Also, public health networks should be considered for disseminating results from trials that have potential for widespread impact. For example, the Cardiovascular Health Council approached the dissemination project to use its network of state public health entities and its ties to both the National Institutes of Health and Centers for Disease Control and Prevention to provide valuable linkages to state high BP initiatives. These types of public health networks could have been valuable partners from the beginning of the project.

Another concern in the recruitment of dissemination partners is the optimal role model for the implementation of persuasive messages aimed at practice change. Theoretically, credible role models would be similar in practice characteristic and perhaps other attributes to the target practitioners [39]. At the same time, they would have characteristics of high status opinion leaders [79]. Some of the IEs for this project were academic physicians while others were community practitioners. Many of them may be opinion leaders in their communities, and they were encouraged to make

presentations to other opinion leaders; however, no attempt was made to assess this type of characteristic in either presenters or participants.

Planning and lead time for strategies

As we have discussed, one suggestion is to recruit dissemination partners early in the trial or even in the trial planning. Another issue is that strategies required longer implementation times than expected. For example, venues approached by IEs often required scheduling six months to a year in advance.

We tried to reach patients by interesting the media in stories for their audiences. This approach may have been more successful on a local level if we had prepared IEs to contact local media as a more central part of their role. Also, media outlets may have been more interested in the dissemination efforts if they had occurred closer to the publication of the ALLHAT results and the release of JNC 7 so that they were seen as newsworthy.

In conclusion, a large multimethod dissemination of clinical trial results is feasible. Woolf (2008) defines two types of translation research activities: the first is the 'bench to bedside' process to use knowledge from basic science endeavors to produce therapeutic modalities for patients while the second type is to ensure that new treatments reach priority populations and are implemented correctly [80]. In the United States, until recently, focus on translation often underemphasized the second, or T2, activities of which the dissemination of the ALLHAT research results is an example. The work presented in this report suggests that planning for such T2 efforts, including evaluation research, should be seriously considered as a part of the funding and design of the clinical trial itself and should begin early in the trial planning process when possible.

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