Impact of the ALLHAT/JNC7 Dissemination Project on Thiazide-Type Diuretic Use

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Background: Strategies are needed to improve the translation of clinical trial results into practice. We assessed the impact of the ALLHAT/JNC7 Dissemination Project’s academic detailing component on thiazide-type diuretic prescribing (ALLHAT indicates Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial; JNC7 indicates the Seventh Report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure).

Methods: We used 2 national databases available from IMS Health: a physician survey of medications reported for hypertension and a pharmacy dispensing database on antihypertensive medications. At a county level, we correlated medication data with Dissemination Project intensity. Practices before the Dissemination Project in 2004 were compared with those after its completion in 2007. We also examined 2000-2008 national trends.

Results: Academic detailing reached 18,524 physicians in 1698 venues via 147 investigator-educators. We noted an association between ALLHAT/JNC7 academic detailing activities and increased prescribing of thiazide-type diuretics. Physician survey data showed that the percentage of hypertension visits where the physician recorded a thiazide-type diuretic increased the most in counties where academic detailing activity was the highest (an increase of 8.6%, from 37.9% to 46.5%) compared with counties where activity was moderate (an increase of 2%) or low (a decrease of 2%), or where there was none (an increase of 2%; P value for trend, <.05). Pharmacy dispensing data showed that thiazide-type diuretic prescribing increased by 8.7% in counties with Dissemination Project activities compared with 3.9% in those without activities (P < .001). Nationally, thiazide-type diuretic use did not increase between 2004 and 2008.

Conclusions: The ALLHAT/JNC7 Dissemination Project was associated with a small effect on thiazide-type diuretic use consistent with its small dose and the potential of external factors to diminish its impact. Academic detailing may increase physicians’ implementation of clinical trial results, thereby making prescribing more consistent with evidence.

Arch Intern Med. 2010;170(10):851-858

ENSURING THAT IMPORTANT clinical trial findings are reflected in the practices of community physicians remains a substantial challenge. Many studies indicate that evidence-based recommendations diffuse into widespread community use only slowly and then incompletely.1-3 This failure to put scientific findings into practice not only compromises societal return on clinical trial investment but also weakens the scientific basis of clinical care.

See Invited Commentary at end of article

Evidence accumulated through national prescribing information suggests that the publication of the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) findings4 had a statistically significant initial impact on prescribing patterns. Following publication of the final ALLHAT results in December 2002, thiazide-type diuretic use increased, calcium channel blocker (CCB) use declined, and angiotensin-converting enzyme (ACE) inhibitor use failed to continue its previous upward trend.5 The incorporation of the ALLHAT results into the December 2003 Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC7) further emphasized that relatively low levels of thiazide-type diuretic prescribing were at odds with evidence-based recommendations.6 Unfortunately, trends in antihypertensive prescribing behavior following ALLHAT and publication of guidelines may not have been sustained.5

Author Affiliations are listed at the end of this article. A list of the ALLHAT Collaborative Research Group Members was published in JAMA. 2002;288(23):2981-2997.
This experience, as well as information from other trials and guidelines, demonstrates that traditional, academically focused modes of clinical trial result dissemination are inadequate. Additional strategies are needed to permanently alter practices to reflect new scientific evidence. A range of alternative approaches has been proposed, including clinical audit, patient empowerment, computerized reminders, pay-for-performance incentives, academic detailing, and continuing medical education. Numerous sources of information suggest that interventions focused on increasing physician knowledge through educational strategies are unlikely to be successful by themselves.8

Academic detailing incorporates many of the approaches used in pharmaceutical marketing.9,11 By using persuasive, individualized small group or one-on-one communication of key points, detailing can summarize findings, suggest concrete changes in practice patterns, and explore potential barriers to change. In addition, by targeting specific physicians recognized as “opinion leaders,” resources can be concentrated on locally influential prescribers. Several systematic reviews have examined the effectiveness of academic detailing in changing clinical practice and found this type of intervention to be effective.9,10,16 The effectiveness of academic detailing is described as ranging from small9 to strong27 with results that are consistently favorable.9,14,17 The effectiveness of academic detailing in affecting prescribing practices is particularly prominent.9,14,17 In this situation, even small changes in prescribing may be important when the population affected is large or where large cost differences exist between alternative medications.9

We set out to evaluate the success of an academic detailing model, a component of the ALLHAT/JNC7 Dissemination Project, in changing national hypertension prescribing practices. Using national US data on antihypertensive prescribing by county and measures of the intensity of ALLHAT/JNC7 academic detailing by county, we hypothesized that increasing local intensity of this intervention would be associated with increased prescribing of thiazide-type diuretics.

To evaluate the impact of the ALLHAT/JNC7 Dissemination Project, we analyzed the relationship between aggregate county information on the extent of academic detailing and temporal changes in thiazide-type diuretic use. Separate analyses were conducted using 2 national databases available from IMS Health (Plymouth Meeting, Pennsylvania): (1) a survey of office-based physicians18 and (2) pharmacy data on medication dispensing.19

ALLHAT/JNC7 DISSEMINATION PROJECT

At the conclusion of the ALLHAT trial, a multicomponent, joint dissemination project of ALLHAT and the JNC7 was implemented. This project focused on extending traditional dissemination approaches by applying novel strategies based on intervention mapping theory23,28 to clinician persuasion, including local academic detailing and broader national scientific and media efforts. Additional details of the ALLHAT/JNC7 Dissemination Project can be found in Bartholomew et al.21

The primary dissemination strategy was to reach prescribers using 147 investigator-educators at 1698 venues. Investigator-educators, mainly clinical investigators from ALLHAT, were chosen based on their ability to recruit and retain ALLHAT participants plus the input of the ALLHAT leadership, especially the regional coordinators. Investigator-educators were recruited to cover most of the United States and to represent its demographic and geographic diversity. They were trained centrally to present ALLHAT results and the JNC7 guidelines as the foundation for achieving blood pressure (BP) control. The main intervention messages were as follows:

1. For most patients, the BP treatment goal is BP lower than 140/90 mm Hg.
2. Most patients diagnosed as having hypertension experience better BP control after adopting lifestyle modifications.
3. Most patients with stage 1 hypertension (BP, 140-159/90-99 mm Hg) experience better BP control and better long-term cardiovascular disease (CVD) risk when taking a thiazide-type diuretic.
4. Most patients with stage 2 hypertension (BP >160/100 mm Hg) experience better BP control and better long-term CVD risk when prescribed a multidrug regimen that includes a thiazide-type diuretic.
5. Most patients with uncontrolled BP benefit from the addition of a thiazide-type diuretic.

Each investigator-educator’s goal was to make 12 presentations over a 12-month period to small, selected groups of key practitioners who prescribe medications for hypertension. At these encounters, the investigator-educators selected from a centrally developed portfolio of training slides. Individualized communication with community physicians was encouraged, including specialized materials such as newsletters, pocket cards summarizing BP control messages, JNC7 reference cards, and other items relevant to CVD risk reduction.21 Press kits also were provided to investigator-educators to use with community media. The ALLHAT/JNC7 dissemination presentations took place beginning in September 2004 and continued through March 2007 and included sites in 41 states plus the District of Columbia. There was substantial variation in the geographic reach of the project, thus creating a natural experiment to explore the correlation between changes in prescribing practice and intervention intensity.

Several secondary project strategies for dissemination included reaching health care providers through professional associations and contacting formularies to encourage antihypertensive prescription according to JNC7 guidelines. Thus, the Dissemination Project had both local and national components aimed at increasing thiazide-type diuretic prescribing.

INTERVENTION INTENSITY

To evaluate the hypothesis that increasing intensity of the ALLHAT/JNC7 Dissemination Project was associated with increasing thiazide-type diuretic use, we identified the extent of local project activities. For each US county, we identified whether any ALLHAT/JNC7 academic detailing efforts had taken place and, if so, the intensity (or dose) of those efforts. Intensity was measured as the number of physician participants contacted by the investigator-educators per 100 000 population members 50 years or older based on year 2000 US Census data.22 Nationally, the project made 1698 presentations to 18 524 physician contacts.21 This equates to a mean effort level of 24 contacts per 100 000 population members 50 years or older for the entire nation and 52 contacts per 100 000 in those 368 counties where dissemination activities occurred. By county, efforts ranged from 0.3 to a high of 5346 with a median of 63.0.
We categorized all US counties into those receiving no efforts (2773 counties with 41.3 million individuals ≥50 years) and those that received any dissemination, among which we created 3 strata of counties by dissemination level. Low-level efforts occurred in 82 counties (target population, 12.2 million) with effort rates ranging from 0.3 to 1.9 clinician contacts per 100,000 population 30 years or older (mean effort rate, 5.3). Moderate-level efforts occurred in 79 counties (target population, 13.1 million) with effort rates ranging from 16 to 48 (mean effort rate, 30). High-level efforts occurred in 207 counties (target population, 10.2 million) with effort rates ranging from 50 to 5546 (mean effort rate, 136).

DATA SOURCES ON PRESCRIBING National Disease and Therapeutic Index

The National Disease and Therapeutic Index (NDTI)18 is a continuing physician survey conducted by IMS Health. The NDTI provides nationally representative diagnostic and prescribing information on patients treated by office-based physicians in the continental United States. A random sample of office-based physicians is selected through random stratified sampling by specialty and geographic region. Approximately 4800 physicians participate each calendar quarter, and each physician is randomly assigned 2 consecutive workdays per quarter for data collection. Physicians provide information on each patient encounter during their data collection period. Over 90% of the hypertension visits occurred in physician offices with the remaining being telephone calls, nursing home visits, and hospital visits. Medication reporting is diagnosis-specific and reflects the physician’s best knowledge of new or continuing medications intended to treat a specific diagnosis. Hypertension visits were reported under the International Classification of Diseases (Ninth Revision) diagnosis code 401.52 We report national estimates that were extrapolated from the sample data for visits by patients of all ages with this diagnosis. With the exception of Hawaii and Alaska, data from at least 1 county were available for all states and the District of Columbia within the NDTI. The sample of NDTI physicians overlapped with dissemination efforts in 176 counties, representing 38 states plus the District of Columbia. The county represents the location of the physician’s office. For each estimate, 95% confidence intervals (CIs) were available via estimates of the relative standard error.

Xponent Database

The IMS Health Xponent database19 consists of a national computerized sample of approximately 36,000 retail pharmacies. These stores, while not a randomly selected subset, are sampled from IMS Health’s pharmacy database, accounting for more than half of all retail pharmacies in the US, and are projected to nationally representative estimates. Pharmacy data are collected daily and reported in monthly aggregates with the prescription as the unit of analysis. The IMS Health Xponent database, covering approximately 70% of retail pharmacy dispensing, provided county-level geographic detail. Commercial mail order pharmacies, which represent 6% of total prescriptions, were not included. With the exception of Hawaii and Alaska, data were available from all states and the District of Columbia, including data from 360 counties where dissemination efforts occurred, representing 41 states plus the District of Columbia. The county represents the location of the pharmacy. National estimates were available representing projections to a national level for drugs dispensed to patients of all ages regardless of diagnosis. For each estimate, 95% CIs were available via estimates of the relative standard error. Of note, estimates from the Xponent were associated with less statistical uncertainty compared with NDTI.

Antihypertensive Medication Classes

We classified physician reporting of antihypertensive medications into 6 drug classes. In particular, we focused on the prescribing of thiazide-type diuretics, including these drugs alone or in combination products. Thiazide-type diuretics included products containing hydrochlorothiazide, chlorthalidone, metolazone, indapamide, methyclothiazide, chlorothiazide, benzthiazide, and trichlormethiazide. In the NDTI data, hydrochlorothiazide accounted for 89% of thiazide-type diuretic use in 2004 and 92% in 2007.

For each database, we used a different metric to assess changes in aggregate thiazide-type diuretic use. For the NDTI survey data, we assessed the likelihood that a patient with treated hypertension was receiving a thiazide-type diuretic: the denominator was the estimate of all visits by patients with hypertension where any treatment was reported, and the numerator was the estimate of visits where a thiazide-type diuretic was reported as part of medication treatment (whether alone or as part of a multidrug regimen). For the Xponent pharmacy dispensing data, we used the volume of thiazide-type diuretic prescriptions as the basis for measuring practice patterns. We calculated the mean number of thiazide-type prescriptions per day per person in the target population of those 50 years or older. For these calculations the number of thiazide-type diuretic prescriptions was divided by the number of days in the period of time being assessed. This quantity was, in turn, divided by the population 50 years or older to arrive at a rate of prescriptions per day per 1000 persons.

While the metrics for assessing practice patterns in the NDTI and Xponent databases are quite distinct, they both aim to assess the use of thiazide-type diuretics relative to patients with hypertension or population members at higher risk for hypertension. Both metrics contrast with alternatives that assess the fraction of all antihypertensive medications that are represented by thiazide-type diuretics. Our metrics, chosen a priori, are more consistent with guideline recommendations and the main message of the ALLHAT/JNC7 Dissemination Project that emphasized that diuretics would frequently be used in combination with other medications.

We also present trend data for all antihypertensive medication classes derived from the NDTI survey. For this analysis, we present the probability that a patient with treated hypertension will be receiving medications in the following classes: thiazide-type diuretics, CCBs, β-adrenergic antagonists, ACE inhibitors, angiotensin II type 1 receptor antagonists, and drugs in all other classes (including centrally acting agents, α-adrenergic antagonists, and other nonthiazide diuretics).
Table 1. Changes in Reported Thiazide-Type Diuretics Among Visits by Patients With Treated Hypertension (TH), IMS Health National Disease and Therapeutic Index

<table>
<thead>
<tr>
<th>Level of Intervention Intensity</th>
<th>Preinterv, Jan-Sep 2004</th>
<th>During Interv, Oct 2004-Feb 2007</th>
<th>Postinterv, Mar-Dec 2007</th>
<th>Change (Preinterv vs Postinterv)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Visits by Patients With TH, mo</td>
<td>Patients With TH Prescribed Thiazides, %</td>
<td>Visits by Patients With TH, mo</td>
<td>Patients With TH Prescribed Thiazides, %</td>
</tr>
<tr>
<td>Counties with no ALLHAT/JNC7 dissemination</td>
<td>19.1</td>
<td>37.1</td>
<td>59.9</td>
<td>38.9</td>
</tr>
<tr>
<td>Counties with any ALLHAT/JNC7 dissemination</td>
<td>18.8</td>
<td>37.1</td>
<td>57.9</td>
<td>37.8</td>
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<tr>
<td>Intensity⁴</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lowest</td>
<td>6.2</td>
<td>38.3</td>
<td>19.0</td>
<td>35.1</td>
</tr>
<tr>
<td>Moderate</td>
<td>6.2</td>
<td>35.2</td>
<td>21.4</td>
<td>36.2</td>
</tr>
<tr>
<td>Highest</td>
<td>6.3</td>
<td>37.9</td>
<td>17.5</td>
<td>42.6</td>
</tr>
<tr>
<td>All of United States</td>
<td>37.9</td>
<td>37.1</td>
<td>117.8</td>
<td>38.4</td>
</tr>
</tbody>
</table>

Abbreviations: ALLHAT, Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial; interv, intervention; Interv, intervention; JNC7, Seventh Report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure; postinterv, postintervention; preinterv, preintervention.

⁴ Lowest, 0.3 to 15.9 clinician contacts per 100 000 population 50 years or older (mean, 5.5 contacts); moderate, 16 to 48 clinician contacts per 100 000 population 50 years or older (mean, 30 contacts); highest, 50 to 5546 clinician contacts per 100 000 population 50 years or older (mean, 136 contacts).

STATISTICAL ANALYSIS

Although a graphical approach was used to evaluate trends in prescribing, we used a predetermined algorithm for evaluating whether the ALLHAT/JNC7 Dissemination Project had resulted in a change in thiazide-type diuretic prescribing. Specifically, we compared prescribing immediately prior to the intervention (January 2004 through September 2004) with prescribing immediately after the completion of the intervention (March 2007 through December 2007). We determined whether changes in prescribing before vs after the intervention were correlated with the intensity of the intervention. Using SAS statistical software (version 9.1; SAS Inc, Cary, North Carolina), we evaluated these differences by a $\chi^2$ test for trend with a $P < .05$ as our level of significance for rejecting the null hypothesis that preintervention vs postintervention change in thiazide-type diuretic prescribing did not differ by level of intervention intensity.

RESULTS

Academic detailing was conducted by 147 investigator educators in 1698 presentations to 18 524 participants in 41 states and the District of Columbia from September 2004 to March 2007.²¹

NATIONAL DISEASE AND THERAPEUTIC INDEX

Among drug-treated visits for hypertension, the likelihood that a thiazide-type diuretic was present among reported therapies increased from 37.1% immediately prior to the intervention (January 2004 through September 2004) to 39.6% following completion of the project (March 2007 through December 2007). Those counties in the highest strata of dissemination efforts experienced the greatest increase in the report of thiazide-type diuretic use with an increase from 37.9% before the intervention to 46.5% after the intervention, a 23% relative increase ($P < .01$). Those counties with lower rates of dissemination efforts were not statistically different from counties not receiving dissemination activities (Table 1). Patterns of thiazide-type diuretic use during the implementation of the intervention were generally intermediate to those observed before and after the intervention (Table 1).

Trend data for the nation as a whole (Figure 1 and Figure 2) indicate the sizable shift in the selection of medications for the treatment of hypertension following the December 2002 publication of the ALLHAT results. Immediately after this time, there was an increase in thiazide-type diuretic use and a decline in ACE-inhibitor use. Overall changes occurring in conjunction with the ALLHAT/JNC7 Dissemination Project suggest a small increase in the use of thiazide-type diuretics. But more prominent, however, are increases in the use of angiotensin II type 1 receptor blockers (ARBs) and decreases in the use of CCB antagonists and ACE inhibitors.

XPONENT DATABASE

The number of thiazide-type diuretic prescriptions dispensed by pharmacists increased nationally from 4.13 prescriptions per day per 1000 persons prior to the ALLHAT/JNC7 Dissemination Project to 4.39 following the project. Those counties receiving any dissemination activities increased from 4.30 to 4.68 over this same time period, an increase of 8.7%. Those counties without activities experienced less marked growth in thiazide-type dispensing (from 3.99 to 4.15, a 3.9% increase; $P < .001$ vs those counties receiving services). There was no clear pattern differentiating changes that occurred among counties receiving different levels of dissemination activities (Table 2). In addition, patterns of dispensing during the intervention (October 2004 through February 2007) varied considerably (Table 2).
Figure 1. Proportion of visits with a drug class reported among patients with drug-treated hypertension. Data are from the IMS Health National Disease and Therapeutic Index, 2000 through 2008.18 ACEI indicates angiotensin-converting enzyme inhibitor; CCB, calcium channel blocker, and ARB, angiotensin II type 1 receptor blocker.

Figure 2. Proportion visits with a drug class reported among patients with drug-treated hypertension. Data are from the IMS Health National Disease and Therapeutic Index, 2000 through 2008.18 “Other classes” indicates α-adrenergic receptor blockers, potassium-sparing diuretics, loop diuretics, and centrally acting agents.

Table 2. Changes in Thiazide-Type Diuretic Pharmacy Dispensing, Thiazide-Type Diuretic Prescriptions (Rx) per Day per 1000 Persons, IMS Health Xponent Database

<table>
<thead>
<tr>
<th>Level of Intervention Intensity</th>
<th>Population &gt;50 y, in Millions</th>
<th>Preinterv, Jan-Sep 2004</th>
<th>During Interv, Oct 2004-Feb 2007</th>
<th>Postinterv, Mar-Dec 2007</th>
<th>Change in Rx Rate (Preinterv vs Postinterv)</th>
<th>Percentage Change in Rx Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Counties with no ALLHAT/JNC7 dissemination</td>
<td>41.3</td>
<td>164.8</td>
<td>178.2</td>
<td>171.2</td>
<td>0.16</td>
<td>3.9</td>
</tr>
<tr>
<td>Counties with any ALLHAT/JNC7 dissemination</td>
<td>35.5</td>
<td>152.8</td>
<td>151.0</td>
<td>166.0</td>
<td>0.37</td>
<td>8.7</td>
</tr>
<tr>
<td>Lowest</td>
<td>12.2</td>
<td>47.6</td>
<td>47.8</td>
<td>51.3</td>
<td>0.30</td>
<td>7.8</td>
</tr>
<tr>
<td>Moderate</td>
<td>13.1</td>
<td>53.1</td>
<td>53.4</td>
<td>58.4</td>
<td>0.40</td>
<td>10.0</td>
</tr>
<tr>
<td>Highest</td>
<td>10.2</td>
<td>52.1</td>
<td>49.7</td>
<td>56.4</td>
<td>0.42</td>
<td>8.1</td>
</tr>
<tr>
<td>All of United States</td>
<td>76.9</td>
<td>317.5</td>
<td>329.2</td>
<td>337.2</td>
<td>0.26</td>
<td>6.2</td>
</tr>
</tbody>
</table>

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a Lowest, 0.3 to 15.9 clinician contacts per 100 000 population 50 years or older (mean, 5.5 contacts); moderate, 16 to 48 clinician contacts per 100 000 population 50 years or older (mean, 30 contacts); highest, 50 to 5546 clinician contacts per 100 000 population 50 years or older (mean, 136 contacts).
We found evidence associating the ALLHAT/JNC7 Dissemination Project with increased use of thiazide-type diuretics in the United States. Although we had hypothesized a graded relationship between intervention intensity and thiazide-type diuretic use, this pattern was evident only in the NDTI physician survey data. Nonetheless, both data sources indicate that diuretic prescribing increased nationally and that counties not receiving the intervention had slower growth in diuretic use when patterns before and after the time frame of the intervention are compared. We acknowledge that this is an ecological association and that counties selected for dissemination efforts may have differed from other counties.

The magnitude of change associated with the intervention is small, likely corresponding to the limited dose of the intervention. The observed pattern of change in thiazide-type diuretic prescribing also differs somewhat between the survey information on prescribing (NDTI) and pharmacy dispensing information (Xponent).

The intervention focused on persuasive communication about prescribing behavior presented by community colleagues, as distinct from an emphasis on clinician knowledge. This strategy used methods known to be effective in academic detailing, including role modeling by peers, visits to individuals or practice groups, and careful delineation of the target behavior. While designed to be more intensive than continuing medical education, the intervention did not include individualized efforts to change prescribing, such as performance standards, behavioral feedback strategies, or practice-based redesign. Greater intensity and individualization might have had a greater impact but would have compromised the national reach of the ALLHAT/JNC7 Dissemination Project. Nonetheless, our findings are consistent with those of past studies of academic detailing and show its potential to motivate changes in physician practices.

Other issues may have blunted the ability of the ALLHAT/JNC7 Dissemination Project to convince community physicians of the relevance of ALLHAT’s population and methods and the applicability of the trial’s findings. The intervention began nearly 2 years after the publication of the ALLHAT summary results, and there was limited opportunity to generate media coverage that might have synergistically magnified the effect of the intervention. During the time period of the intervention, several other clinical trials were published that were promoted as casting doubt on the role of thiazide-type diuretics. This may have complicated the messages delivered by the intervention and reduced the likelihood of prescribing changes. Similarly, there was substantial questioning of the ALLHAT findings by recognized hypertension authorities, as well as by the pharmaceutical industry, that likely reduced the potential impact of the results on clinical practice. For example, unwarranted concerns regarding the use of thiazide-type diuretics in patients with diabetes mellitus may have hampered efforts to alter prescribing practices. ALLHAT leaders, however, have published multiple commentaries in high-prestige journals that enumerate counterarguments to such criticisms.

While the ALLHAT/JNC7 Dissemination Project may have increased the use of thiazide-type diuretics, other changes in prescribing practices are less consistent with evidence. In particular, the continued increase in the use of ARBs and the decrease in ACE inhibitors and CCBs represent trends that are not congruent with the accumulated evidence on outcomes. These changes add substantially to the cost of hypertension treatment, especially given the recent availability of multiple generic ACE inhibitors and CCBs.

The findings of this study should be interpreted cautiously in the context of the following limitations. This was an ecological analysis conducted at the level of US counties, and any association does not necessarily imply a causal relationship between the ALLHAT/JNC7 Dissemination Project and changing patterns of thiazide-type diuretic use. Furthermore, the sites selected for investigator-educator activities were not selected randomly and may differ from those in other geographic areas. Despite this potential, the nonrandom allocation of counties to differing intensity levels of the intervention is unlikely to explain our results. Investigator-educators were selected based on their interest, and neither these physicians nor project staff were aware of baseline patterns of thiazide-type diuretic use. Specific efforts were made to select a geographically diverse panel of investigator-educators.

Use of data for the population 50 years or older in the Xponent analysis provides an inexact proxy for the population with hypertension. There also may be substantial variation induced by other geographically varying factors (eg, drug promotion of nonthiazides), as well as variation connected with the measurement of prescribing patterns. This variation may have made it difficult to detect a more sizeable effect of the ALLHAT/JNC7 Dissemination Project and may account, in part, for the differences in findings between the 2 data sources.

The NDTI and Xponent are different data sources and represent distinct populations that might differ in their response to the intervention. The NDTI data on office visits by patients with hypertension will overrepresent patients making frequent physician visits, including those requiring changes in their medications. Xponent, representing pharmacy data on new and refilled antihypertensive medications, will include patients treated with these drugs for reasons other than hypertension. To a greater extent than NDTI, Xponent will reflect patterns of refilling and discontinuation influenced by factors beyond physicians’ control. These 2 sources of information also differ in the metric of measuring diuretic use and potential biases. Dissemination efforts were coded by physician office location in NDTI and pharmacy location in Xponent. With their advantages and disadvantages, the use of NDTI and Xponent together provides some degree of cross-validation given their largely concordant results.

Although other explanations cannot be excluded, there was a statistically significant increase in thiazide-type diuretic prescribing that was geographically associated with clinical investigator–centered academic detailing aimed at in-
creasing use of thiazide-type diuretics. These dissemination efforts focused on the implementation of guidelines derived from the ALLHAT findings but also emphasized the role of thiazide-type diuretics in patients requiring multiple medications. Corresponding to the minimal intervention dose, the effect of the ALLHAT/JNC7 Dissemination Project is small. In addition, other factors, including controversy regarding the appropriate role of thiazide-type diuretics, may have blunted the intervention’s impact. Academic detailing has the potential to improve prescribing patterns but may require greater intensity to facilitate translation of clinical trials evidence into community practice.

Accepted for Publication: December 10, 2009.

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Author Contributions: Dr Stafford had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Stafford, Bartholomew, Cushman, Cutler, Einhorn, and Piller. Acquisition of data: Stafford, Davis, and Pressel. Analysis and interpretation of data: Stafford, Bartholomew, Cushman, Cutler, Davis, Dawson, Einhorn, Furberg, Piller, and Whelton. Drafting of the manuscript: Stafford, Bartholomew, Cutler, Davis, and Einhorn. Critical revision of the manuscript for important intellectual content: Stafford, Bartholomew, Cushman, Cutler, Davis, Dawson, Einhorn, Furberg, Piller, Pressel, and Whelton. Statistical analysis: Stafford. Obtained funding: Stafford, Davis, Einhorn, and Pressel. Administrative, technical, and material support: Stafford, Bartholomew, Cutler, Davis, Dawson, Furberg, Piller, Pressel, and Whelton. Study supervision: Stafford, Davis, and Einhorn.

Financial Disclosure: Dr Stafford has been a consultant for Bayer Corp and has had grants and/or contracts with Procter and Gamble, GlaxoSmithKline, Toyo Shinyaku, and Wako. Dr Cushman has been a consultant for Abbott Laboratories, Bristol-Myers Squibb, Calpis, Daichi Sankyo, Forest Pharmaceuticals, Gilead Colorado, Johnson & Johnson, King, Myogen, Novartis, Pfizer Inc, Pharmacopeia, Reddy Pharmaceuticals, Roche, Sankyo, Sanofi-Aventis, Sanofi-Synthelabo, Sciele, and Takeda; has received honoraria from Astra-Zeneca, Boehringer Ingelheim, Forest Pharmaceuticals, King, Novartis, Pfizer Inc, Sankyo, Sanofi-Aventis, and Sciele; and has had grants and contracts with Abbott Laboratories, Astra-Zeneca, Biovail, King, and Novartis. Dr Davis has held financial interest in Amgen and has consulted for BioMarin, Forest Pharmaceuticals, GlaxoSmithKline, Merck, Proctor and Gamble, and Takeda. Dr Furberg has received honoraria from Novartis, Sanofi-Synthelabo, and Wyeth; has had grants and contracts with GlaxoSmithKline; and has been on the board of directors for Wyeth.

Funding/Support: This study was supported by contract N01-HC-35130 from the National Heart, Lung, and Blood Institute (NHLBI), as well as an NHLBI mentoring award (RSS, K24HL086703). The ALLHAT Investigators acknowledge contributions of study medications supplied by Pfizer Inc (amlodipine), AstraZeneca (atenolol and lisinopril), and Bristol-Myers Squibb (pravastatin) and financial support provided by Pfizer Inc. The statements, findings, conclusions, views, and opinions contained and expressed in this article are based in part on data obtained under license from the following IMS Health Inc information services: National Disease and Therapeutic Index (2000-2008) and Xponent (2004-2007), IMS Health Inc.

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The Final Translational Hurdle

The connection between clinical research and typical patient care presents a frustrating paradox. Many well-documented advances in therapy are not adopted widely or quickly, whereas other, unimpressive new treatments are taken up in epidemic proportions, their use often fueled by marketing campaigns that are far more powerful than the medicines being advertised. As a result, patients are frequently exposed to new therapies that may be less effective or less safe than the older regimens they replace. For example, ezetimibe (Zetia and Vytorin; Merck & Co Inc, Whitehouse Station, New Jersey) nearly doubled the occurrence of myocardial infarction or stroke in patients who took it, while offering no greater analgesic efficacy than older nonsteroidal anti-inflammatory drugs, such as naproxen sodium. The lavish promotion that drives such overuse is reserved for the most expensive drugs, because only a high-priced product can provide its manufacturer with the economic benefit to justify a big marketing campaign. Patients are left to bear the burden of the mediocre efficacy or increased risk of these products, while all of us get to pay for their high cost.

This situation is especially vexing when there is solid evidence from well-conducted randomized trials that should guide therapy but does not. The treatment of hypertension is a striking example of this problem. During the late 1980s and 1990s, it seemed as if the more trial evidence that was published documenting the efficacy of thiazide-type diuretics in treating blood pressure, the smaller the market share of these drugs became. The problem was not the adequacy or relevance of these trials, nor the persistence of clinicians’ old habits of care—because use of thiazides was often the very habit that nor the persistence of clinicians old habits of care—because use of thiazides was often the very habit that was being displaced. Nor was it the failure of the scientific community to enunciate clear, evidence-based recommendations about therapy, as represented by the JNC7. Rather, it was the growing dominance of marketing-based communication suggesting that these drugs were “old-fashioned” and should be displaced by the more “modern” treatments of CCBs and ACE inhibitors as initial therapy for patients with uncomplicated hypertension. Changes in hypertension treatment during these years provide compelling evidence of the power of commercially driven research and promotion to drive practice.

Despite the recent upsurge of interest in translational research—moving a basic science discovery from the laboratory to drug development and evaluation—far less attention has been paid to the final translational hurdle: ensuring that the results of well-conducted clinical research are applied to typical patient care. This is the important agenda that Stafford et al have attempted to address in their article.