An Intervention to Improve Secondary Prevention of Coronary Heart Disease

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Background: Translating guidelines into clinical practice has proved to be quite difficult, even when the guidelines are well accepted and noncontroversial. Both computerized reminders and academic detailing have been effective in changing physician prescribing behavior. In this study, we sought to use these methods, mediated by clinical pharmacists, to improve adherence to the secondary prevention guidelines in hospitalized patients with myocardial infarction.

Methods: A randomized, prospective study was performed in which computerized alerts identifying hospitalized patients with elevated troponin I levels were routed to clinical pharmacists. The pharmacists then conducted academic detailing for physicians caring for patients with acute myocardial infarction who were randomized to the intervention group. Patients in the control group received standard care. The main outcome measure was the proportion of patients discharged on a regimen of aspirin, β-blockers, angiotensin-converting enzyme inhibitors, and statins.

Results: The intervention had a significant impact on the proportion of patients discharged on a regimen of angiotensin-converting enzyme inhibitors (328/365 [89.9%] vs 409/488 [83.8%], intervention vs control, respectively, P=.02), and statins (344/365 [94.2%] vs 436/488 [89.3%], P=.02). There was no statistical impact on β-blocker (350/365 [95.9%] vs 448/488 [91.8%], P=.10) or aspirin use (352/365 [96.4%] vs 471/488 [96.5%], P=.87). When all 4 classes were considered together, 305 (83.6%) of 365 patients vs 343 (70.3%) of 488 patients were discharged on a regimen of all secondary prevention medications to which they did not have a contraindication (P<.001).

Conclusion: A computerized alert with pharmacist-mediated academic detailing is an effective means to increase adherence to secondary prevention guidelines for coronary heart disease.

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Department of Medicine, Washington University School of Medicine, (Drs Bailey, Braverman, Goldberg, and Dunagan and Ms Noirot), Department of Pharmacy, Barnes-Jewish Hospital (Drs Blickensderfer, Rachmiel, Schaiff, and Kessels), and BJCCare, is a 1385-bed teaching hospital affiliated with the Washington University School of Medicine, St Louis, Mo. The organization of the BJH medical service into “firms” allowed 4 groups of internal medicine physicians (each

Clinical Practice Guidelines

Clinical practice guidelines are intended to assist practitioners and patients in making decisions about appropriate health care. However, translating guidelines into clinical practice has proved quite difficult, even when the guidelines are well accepted and noncontroversial. Aspirin, β-blockers, angiotensin-converting enzyme (ACE) inhibitors, and lipid-lowering agents have significant morbidity and mortality benefits for patients after an acute myocardial infarction, but these agents are not optimally used. The American College of Cardiology and the American Heart Association have published guidelines for the treatment and secondary prevention of acute myocardial infarction, which include recommendations for the use of aspirin, β-blockers, ACE inhibitors, and lipid-lowering agents. The National Cholesterol Education Program also has published guidelines for the diagnosis, evaluation, and treatment of high blood cholesterol levels in adults.

Among the more promising strategies for changing physician behaviors are academic detailing and reminders. Increasingly, computer-generated reminders are also proving to be an effective means of changing physician behavior. In this study, we sought to use these methods mediated by clinical pharmacists to improve adherence to the secondary prevention guidelines in hospitalized patients with myocardial infarction.
comprising interns, residents, and attending physicians) to be assigned to intervention and control groups. Patients who are new to BJH are randomly assigned to the firms by the admitting office. Thereafter, they remain assigned to the same firm. Before the study began, the BJH laboratory instituted a policy of performing a lipid profile on all blood samples obtained within 24 hours of admission that had elevated troponin I levels. This policy assured that all physicians had lipid profile information available to them for these patients.

The Medical Informatics Laboratory maintains a real-time database that includes patient admission, discharge and transfer data, laboratory information, and diagnoses. Patients with elevated troponin I levels (>1.4 ng/mL) occurring within the first 24 hours of admission were identified using this database, and a clinical pharmacist was notified with this information via a daily secure e-mail list. The pharmacists then assessed (1) whether the patient was eligible for intervention; (2) whether the patient was assigned to control or intervention firms; and (3) whether the patient was receiving the full complement of medications for secondary prevention of coronary heart disease and, if not, whether there were documented contraindications for nonprescribed medications. The pharmacists then contacted physicians caring for intervention candidates on intervention firms to recommend secondary prevention medications. Pharmacists with patients with elevated troponin I levels that occurred on nonmedical services were randomized according to their primary care internists' or consulting cardiologist's firm.

Study exclusions were explicitly defined before study initiation. Patient level exclusions included patient death during the study admission; terminal comorbidity or do-not-resuscitate status; perioperative or periprocedural increases in troponin I levels; patient transfers from outside hospitals in which the infarct event occurred more than 24 hours before admission to BJH or patient transfers to outside hospitals before intervention could be undertaken; patients discharged against medical advice; and patients with increases in troponin I levels that were not caused by coronary heart disease, as determined by the patients' care team.

Pharmacists contacted physicians with secondary prevention recommendations in the intervention group, while control group patients were simply observed, with notation of exclusions for individual drug classes. The interactions between the pharmacists and physicians were either in the form of face-to-face discussions or took place by telephone. During this interaction, the evidence base for the recommendations was discussed and a plan of action was determined. Pharmacists then followed up on a daily basis to confirm that the agreed-upon plan of action was implemented. Drug class exclusions were also explicitly defined before study initiation. Exclusions for aspirin intervention included active bleeding in the gastrointestinal tract, allergy, treatment with clopidogrel, or documented intolerance. Exclusions for intervention with ACE inhibitors included a serum creatinine level greater than 2.5 mg/dL (221 µmol/L); treatment with an angiotensin receptor blocker or enrollment in a study involving these agents; unacceptable cost to the patient; systolic blood pressure less than 100 mm Hg; or documented intolerance. Exclusions for intervention with β-blockers included treatment with scheduled bronchodilators or inhaled steroids; a heart rate of less than 60 beats/min; acute symptomatic heart failure; or documented intolerance. Exclusions for statins included a baseline low-density lipoprotein cholesterol (LDL-C) level less than 100 mg/dL (≤2.59 mmol/L); a baseline aspartate aminotransferase level greater than twice the upper limit of normal; unacceptable cost to the patient; or documented intolerance.

Sample size estimates were determined before initiation of the study and were based on the estimated number of individuals with LDL-C levels greater than or equal to 130 mg/dL (≥3.37 mmol/L) that were required to detect an increase in the rate of prescription of lipid-lowering therapy from a historical baseline of 67% to a target of 80%, with β = .80 and a 2-tailed α = .05. The use of lipid-lowering therapy was chosen because we could most precisely determine candidacy for these drugs from existing data. From historical data, we also determined that approximately 360 patients would be enrolled in each arm of the study over an 18-month period. Based on historical data, the 2 firms with the highest and lowest rates of statin use were paired together for the study, and the 2 firms with intermediate rates of statin use were paired together. Intervention and control groups, 2 firms in each group, were then assigned by a coin toss.

We conducted 2 sets of analyses to examine the impact of the intervention: for the first set, we omitted from the denominator those patients with exclusions for individual drug classes; for the second, we performed an intention-to-treat analysis that included all patients. For both sets of analyses, we first used the χ² test to examine crude differences between the intervention and the control groups in the proportions of patients discharged on a regimen of secondary prevention medications. Because the P values for this analysis were potentially biased owing to the group-randomized nature of the study, we used GLIMMIX, a macro for fitting generalized linear mixed models, to evaluate whether observed differences in the outcome measures between the groups were statistically significant.

In these models, we treated the study assignment variable as a fixed physician-level effect, and the discharge physician was coded as a nested random effect. Models were fitted with and without fixed patient-level effects of age, sex, race, and presence or absence of malignancy as a comorbidity. All analyses were performed with SAS for Windows, version 8.02 (SAS Institute Inc, Cary, NC).

Because of changes in the organization of firm system on the medical service at BJH slated for June 23, 2001, the study was terminated with fewer patients than originally planned. Between February 1, 2000, and May 31, 2001, we identified 1540 inpatients who had an internal medicine firm assignment and an elevated troponin I level within 24 hours of admission. Of these, 895 patients (58%) were considered eligible for the study and were assigned to intervention and control groups on the basis of their firm assignment.

A total of 216 discharge physicians were involved in the study. Although little overlap of physicians treating patients in more than 1 firm was expected, this crossover phenomenon did take place. Contamination of the intervention or control group was a concern in 42 patients: 27 patients in the intervention group were treated by physicians assigned to a control firm, and 15 patients in the control group were treated by physicians assigned to an intervention firm. These cases were deleted from further analysis. Thus, the final analytical sample was based on 853 patients, 488 (57%) of whom were assigned to the control group and 365 (43%) of whom were assigned to the intervention group. Reasons for exclusion are shown in Table 1. Demographic characteristics of the 853 study patients are shown in Table 2. The intervention and control groups did not differ by sex, race, or age quartile. The intervention group included a slightly

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**RESULTS**

Because of changes in the organization of firm system on the medical service at BJH slated for June 23, 2001, the study was terminated with fewer patients than originally planned. Between February 1, 2000, and May 31, 2001, we identified 1540 inpatients who had an internal medicine firm assignment and an elevated troponin I level within 24 hours of admission. Of these, 895 patients (58%) were considered eligible for the study and were assigned to intervention and control groups on the basis of their firm assignment.

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larger number of patients with a comorbidity of malignancy. Characteristics of the discharge physicians are shown in Table 3. There were no statistical differences in these characteristics between the intervention and the control groups.  

The impact of the intervention on the prescription of secondary prevention medications for coronary heart disease at hospital discharge is shown in Table 4. The intervention was associated with a statistically signifi-
than is reasoned advice from a clinician colleague. Also, many CPOE systems are geared around admission order sets, whereas the strategy used by our study could also be used to identify people who have a myocardial infarction at a later stage of the hospitalization. Approaches to guideline adherence are needed that fill the gap while CPOE clinical decision support technology is maturing and that will reinforce a computer’s advice with a human component.

In this study, we have shown that a system of computerized screening of hospitalized patients to find potential candidates for secondary prevention medications for coronary heart disease, coupled with pharmacist-mediated academic detailing of physicians caring for these patients, significantly improved physician adherence to established guidelines for using these medications. With ongoing regulatory pressures to improve care of patients with coronary heart disease, our approach could be a model for increasing adherence to evidence-based guidelines, including those for coronary heart disease and other guidelines.

A variety of other strategies for improving guideline adherence have been suggested. Approaches involving physician opinion leaders using a broad education campaign, printed guideline algorithms, and preprinted order sets have been successful at both academic and nonacademic centers in nonrandomized studies. The importance of attaining these gains in guideline adherence is underscored by the mortality benefit that can be achieved by participants in these programs. Similar approaches have also worked for other cardiovascular conditions. This approach has led to web-based interventions that are available to assist hospitals to improve their adherence to national guidelines for the secondary prevention of coronary heart disease and for the care of patients with congestive heart failure. Such strategies, as well as those used in our study, have been shown to be more potent for facilitating guideline adoption than traditional methods such as didactic lectures, traditional continuing medical education, and mailings.

In the wake of the performance monitoring required by national accrediting agencies, and public recording of these data, many institutions are reporting very high rates of adherence to secondary prevention guidelines, in many cases higher than those achieved with our intervention. However, these reported rates focus on patients with a principal International Classification of Diseases, Ninth Revision, code of acute myocardial infarction. Because International Classification of Diseases, Ninth Revision, codes are assigned retrospectively, and our study involved prospective identification of candidates, the populations being reported are not equivalent. Although we can only speculate as to the approaches that are being used to achieve very high rates of adherence, it is likely that many of them involve labor-intensive or inefficient approaches that will be difficult to scale to other conditions as more and more evidence-based practices are identified and correspondingly implemented. Our approach efficiently identifies candidate patients, focusing the efforts on those patients who appear to be candidates but who are not receiving the full complement of secondary prevention medications. This approach should be adaptable to other conditions as these mandates to measure performance are issued. Finally, our approach serves as a “safety net” to identify patients that may slip through any front-end approach to improve guideline adherence.

Our study has certain limitations. First, our study was conducted at an academic medical center, which may limit the generalizability of our findings to other health care settings. Second, the intervention took place as a formal study, and its performance may differ when implemented in a “real world” setting. However, since the completion of this study, we have seen persistent improvements in guideline adherence using the methods described in this study. Third, we did not include some patients who may have benefited from the intervention. For example, automated detection of elevation in troponin I levels was the mechanism for identifying potential candidates for intervention. Therefore, patients with acute coronary syndromes or established coronary heart disease without an elevated troponin I level were not included in our study. Similarly, we were only able to detect measurements of troponin I levels that were performed within our health care system. Therefore, a patient with an elevated troponin I level that occurred at another institution before transfer would not have been detected and may also have resulted in a missed opportunity for intervention. Also, some of the medication level exclusions were relative rather than absolute contraindications. Therefore, some of these excluded patients could have benefited from the intervention. Fourth, the

### Table 4. Proportion of Eligible Patients Discharged on a Regimen of Secondary Prevention Medications

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Control Group (n = 488)</th>
<th>Intervention Group (n = 365)</th>
<th>P Value*</th>
<th>P Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE inhibitor</td>
<td>409 (83.8)</td>
<td>328 (89.9)</td>
<td>.01</td>
<td>.02</td>
</tr>
<tr>
<td>Aspirin</td>
<td>471 (96.5)</td>
<td>352 (96.4)</td>
<td>.95</td>
<td>.87</td>
</tr>
<tr>
<td>β-Blocker</td>
<td>448 (91.8)</td>
<td>350 (95.9)</td>
<td>.08</td>
<td>.10</td>
</tr>
<tr>
<td>Statin</td>
<td>436 (89.3)</td>
<td>344 (94.2)</td>
<td>.01</td>
<td>.02</td>
</tr>
<tr>
<td>All 4 classes</td>
<td>343 (70.3)</td>
<td>305 (83.6)</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Abbreviation: ACE, angiotensin-converting enzyme.

*P value for intervention effect derived from generalized linear regression model.
†P value for intervention effect adjusted for individual-level effects of age, race, sex, and malignancy diagnosis.
resources, both technical and clinical, to design and implement this approach were considerable and may not be practical in settings lacking these resources. However, now that the investment has been made in our setting, the infrastructure is available for expansion to guidelines governing other conditions. It is possible that another approach, such as standardized order sets, could be more cost-effective. However, we have found such approaches difficult to sustain in our environment, and such an approach would require continual reinforcement to maintain effectiveness. Finally, at the time of this study, lipid-lowering therapy was recommended for secondary prevention of coronary heart disease in patients with an LDL-C level greater than or equal to 130 mg/dL (≥3.37 mmol/L). The current threshold for lipid-lowering therapy is an LDL-C level of 100 mg/dL or higher (≥2.59 mmol/L), with an optional LDL-C threshold greater than 70 mg/dL (>1.81 mmol/L) for high-risk patients. These changes were easily incorporated in our current approach.

Additional study is needed to test the generalizability, feasibility, and sustainability of our system for improving guideline adherence for established coronary heart disease, as well as other conditions, both in its current setting and in nonacademic community hospitals.

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Author Contributions: Dr Bailey had full access to all of 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: Bailey, Blickensderfer, Goldberg, Dunagan. Acquisition of data: Noirot, Blickensderfer, Rachmiel, Schaff, Kessels. Analysis and interpretation of data: Bailey, Waterman, Dunagan. Drafting of the manuscript: Bailey. Critical revision of the manuscript for important intellectual content: Bailey, Noirot, Blickensderfer, Rachmiel, Schaff, Kessels, Braverman, Goldberg, Waterman, Dunagan. Statistical analysis: Waterman. Obtained funding: Bailey, Dunagan. Administrative, technical, and material support: Noirot, Blickensderfer, Rachmiel, Schaff, Kessels. Study supervision: Bailey.

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