Editorial

Improving the Pathway From Cardiovascular Medication Prescribing to Longer-Term Adherence
New Results About Old Issues

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Medications are the cornerstone of the treatment and prevention of coronary heart disease. More than 40% of the decline in coronary heart disease mortality observed over the past decades has been attributed to the application of evidence-based drug therapies.1 To maximize the benefits that these drugs offer, a cascade of events from appropriate prescribing to longer-term adherence must be successfully performed. As with most multistep processes, lesions at numerous points on this pathway have been appreciated for many years.2 Although the efforts of professional societies3 and credentialing bodies4 have improved medication use in high-risk patients discharged from hospital, other guideline-recommended therapies continue to be substantially underprescribed4 and long-term adherence with these therapies remains suboptimal.5

Two studies in this issue of Circulation: Cardiovascular Quality and Outcomes provide new and important data about these old issues. Nasir et al6 studied the relationship between coronary artery calcium scores (CACS) and the use of lipid-lowering medication, antihypertensives, and aspirin in patients without known coronary artery disease. CACS results (and their interpretation) were provided to patients and the majority of their physicians. The investigators found that patients with higher CACS (especially >400) were more likely to be started on treatment. CACS scores were also associated with medication continuation, although the strength of this association was somewhat weaker.

Although the relationship between CACS results and medication use is intriguing, the study’s most important findings relate to the underuse of evidence-based therapies. At baseline, 15% of patients with LDL levels above National Cholesterol Education Program (NCEP) treatment thresholds were not receiving lipid-lowering therapy. More notable, 31% of patients eligible for blood pressure lowering based on Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) recommendations and an equal proportion of patients eligible for aspirin based on American Heart Association (AHA) guidelines were not receiving these therapies. Although the study time period overlapped with the publication dates of these guidelines, basic recommendations for primary prevention have not changed dramatically for many years, and therefore the results of Nasir et al are very consistent with the existing literature about missed opportunities for prevention.

This study also demonstrates the somewhat fine balance between “underuse” and “overuse” of medical therapies and thus has implications for efforts to improve health care quality. As expected, the use of primary prevention increased over time in patients who were considered appropriate candidates for treatment. However, after receiving CACS results, a substantial proportion of patients for whom guidelines do not recommend therapy were also started on these treatments. For example, among patients with a CACS >400, aspirin was started in 33% of guideline-appropriate and 29% of guideline-inappropriate cases. Some patients may have started aspirin because they had a vascular event or developed some other clearer indication for treatment (and unfortunately the absence of a control group makes it impossible to estimate the magnitude of these effects). It is also likely that the CACS results drew greater attention to cardiovascular prevention and/or the added information tipped the balance in favor of treatment in those cases where there was uncertainty. Although patients with higher CACS are more likely to have cardiovascular events,7 there is no evidence demonstrating the value of treatment initiated on this basis and thus these “overtreated” patients may have been exposed to the risks of aspirin without any of its benefits.

Lipska et al8 assessed the consequences of appropriate medication use further down the prescribing cascade. They evaluated the impact of medication discontinuation at discharge in patients hospitalized for acute myocardial infarction and found that the 13% of patients in whom oral hypoglycemics or insulin were stopped were 30% more likely to die over the subsequent year than patients for whom these medications were continued. These findings are not necessarily surprising—reductions in the use of “essential” medications should have adverse clinical consequences and numerous previous studies have demonstrated this association.9 For example, patients who discontinue evidence-based medications after an acute myocardial infarction10 or stroke11 are much more likely to die than patients who remain adherent. Lipska et al add to this literature by studying medications for

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diabetes, whose role in preventing (and causing) cardiovascular disease and mortality has evolved over the past decade.

That said, given the absence of evidence supporting the ability of tight glycemic control to reduce mortality in patients with established coronary disease,\textsuperscript{12} the magnitude of effect that these investigators observed is larger than might plausibly be true. If the use of diabetes medications for patients with coronary disease does not decrease mortality (and may in fact increase it) why should stopping these medications cause death? Although there are potential physiological explanations, especially in the immediate post–myocardial infarction time period, the results of the Lipska et al study may have more to do with why medication was discontinued rather than the consequences of discontinuation itself.

This phenomenon is known as the “sick stopper bias” and is based on the observation that patients who stop therapy are often sicker than patients who do not, either because of true clinical differences or their lower likelihood of engaging in healthy activities. This is the converse of the “healthy user effect,” whereby patients who adhere to preventive therapies are more likely than nonadherent patients to engage in a broad spectrum of healthy behaviors, such as the use of preventive services\textsuperscript{13} and, as a result, are less likely to have adverse health outcomes that are both related and unrelated (eg, motor vehicle accidents) to the therapeutic effects of the drugs being evaluated.\textsuperscript{14} In this way, the apparent association between medication discontinuation and adverse clinical outcomes may actually be due to confounding by health status and/or healthy practices, even in analyses that use multivariable models to carefully adjust for observable covariates.

In the Lipska et al study, patients whose diabetes medications were discontinued were sicker (for example, they had more comorbid conditions and worse left ventricular systolic function) and received lower quality health care (for example, they were less likely to have undergone revascularization or to have been prescribed secondary prevention medications at discharge). Both factors may have confounded their analysis.

The authors were careful to acknowledge the potential for unmeasured confounding and performed stratified analyses in an attempt to address this bias. Future investigations may use newer approaches including high-dimensional propensity scores\textsuperscript{15} or instrumental variable methods,\textsuperscript{16} or even simply including markers of health-seeking behavior, such as the receipt of immunizations\textsuperscript{17} or adherence to other medications,\textsuperscript{18} as parameters in their regression analyses.

Notwithstanding their methodological limitations, the findings of both Lipska and Nasir have substantial more efficient health improvement strategy that guarantees quality improvement and offers the potential to reduce health care costs.\textsuperscript{20} Of course, the challenge is to develop interventions that effectively address the myriad of reasons for these suboptimal practices. This is not different from the problem that evidence-based medications themselves are used to treat—they are only part of a multifaceted regimen for cardiovascular risk reduction. Thus, to improve their overall use, we must consider and address lesions along the entire pathway from medication prescribing to longer-term adherence.

Disclosures

Dr Choudhry provides consultative services on appropriate medication use to The Alosa Foundation, a nonprofit 501c3 educational organization with no relationship to any drug or device manufacturers (amount ≥$10 000).

References


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