

Polypharmacy and Medication Adherence

Small Steps on a Long Road

Three papers in this issue address the related problems of polypharmacy^{1,2} and medication adherence.³ A common theme is the investigation of specific patient populations at risk of complex medication regimens and compromised adherence. Patients who are hospitalized, elderly, or afflicted with HIV all take numerous medications. Besides the sheer number of medications, additional factors that may interfere with adherence include the changes in drug regimens that occur during hospitalization, cognitive and functional impairment associated with aging, and concurrent substance abuse. One limitation common to all three studies is that patient perceptions and outcomes were not assessed. Moreover, group comparisons in all three studies revealed differences that frankly must be gauged as modest rather than substantial.

Admission to the hospital is a known risk factor for increasing the numbers of appropriate and inappropriate medications⁴ as well as errors in patients' medication regimens.⁵ Muir et al.¹ demonstrated that providing residents with a simple calendar of the days of the week and medication administration times for each admitted patient taking five or more drugs reduced both the number of medications and daily doses. Reducing the numbers of inappropriate medications is particularly important for medically ill or older adults who each day must manage inordinate numbers of drug products.^{6,7} Therefore, simple interventions in the controlled environment of the hospital would be welcome.

However, it should not be presumed that simply decreasing the number of medications will automatically translate into favorable patient outcomes. Few would argue about the benefits of reducing the use of amitriptyline among older adults. However, not all reductions in central nervous system, gastrointestinal, or respiratory drugs, hormones, antibiotics, or other medications may be equally warranted. Further, care must be taken that the timing of discontinuations of some medications such as central nervous system depressants does not lead to withdrawal reactions shortly after discharge.^{8,9} Finally, postdischarge follow-up is needed to establish whether simplified regimens are sustained by the primary care provider and to monitor for adverse consequences of changing drug regimens.⁵

Muir et al. did not randomize physicians because blinding was not possible and therefore contamination across teams would have been a distinct possibility. However, a randomized controlled trial by Smith et al. failed to show a reduction in polypharmacy when physicians were provided a list of their patients' outpatient medications.¹⁰ While residents and interns did not return to study ward services in the trial of Muir et al. it is

uncertain whether some faculty may have attended on more than one rotation and, if so, whether this may have had any influence on the findings. Also, patients in the control group had a greater mean number of discharge diagnoses compared to the intervention group (8.4 vs 7.8), and sicker patients may truly need more medication. However, medical comorbidity as a potential confounder does not entirely explain away the intervention's efficacy since group differences persisted even after adjustment for the number of discharge diagnoses.

Learning what drugs patients are actually taking is an enormous problem in therapeutics. The list of medications found within the paper chart is often limited to recently prescribed medication whereas in their homes patients have access to previously prescribed drugs, over-the-counter (OTC) medications, and alternative drugs. The relevance of knowing exactly what drugs patients take is highlighted by patients receiving duplicate drugs such as nonsteroidal anti-inflammatory drugs from prescription and over-the-counter sources,¹¹ adverse cardiovascular events caused by phenylpropranolamine,¹² and hazardous drug interactions involving herbal drugs such as St. John's Wort.¹³

Where can physicians find the most accurate, comprehensive, and current drug list for patients? Yang et al. found that medication lists generated by asking patients to bring in all their medications during a clinic visit are in perfect agreement with regimens documented during a home visit only about half the time.² While this study may be interpreted by some as discrediting the "brown bag" approach, the majority of omissions from the clinic visit list were vitamins, minerals, and herbal remedies rather than prescription drugs. Also, the home visit medication list was generated using a semistructured interview by an investigator whose sole agenda was to ascertain medications. In contrast, medications were elicited during the clinic visit in a nonstandardized fashion by geriatricians who were evaluating patients as new referrals for one or more medical problems. How much of the difference between the clinic and home list is attributable to a more structured interview and fewer competing demands (neither of which require an actual home visit) rather than the "home search" itself is not certain.

Given the current circumstances of poor information on medication use,¹⁴ what are the prospects for physicians obtaining more accurate lists of medications for their patients? Resources permitting, two options are visiting home nurses and community pharmacists. Nurses often assist patients in maintaining lists of their medications in patients' homes. However, this service is available only to a small fraction of patients for whom lists are needed, and getting the drug lists to primary care physicians is

difficult. In contrast, practically all pharmacies have computerized prescription services. Pharmacists are quite familiar with the various types of prescription and non-prescription drug products. With modest programming of computers, pharmacies could provide physicians with regularly updated lists of drugs for patients at a reasonable cost.

Though some pharmacists would argue that such a service is not available with the software they are using, we would argue that it should be. Such lists could include nonprescription drugs for bar-coded products if products could be mapped to a specific patient. The compiled list of a patient's current drug use could be automatically encrypted and e-mailed to the physician's office each time the patient's drug profile changes. Physicians or authorized office personnel could open the file using a password that is unique to that office. Fear of the loss of patient privacy and confidentiality should not be a barrier; obviously, patient consent to such a process should be provided and documented. Yet, prescription data already passes from most pharmacies to pharmacy benefit managers electronically to adjudicate insurance claims. Why not put informatics to work for sound clinical reasons as well as financial reasons?

Adherence to a medication regimen depends on prospective and retrospective memory.¹⁵ Prospective memory helps the patient remember to take the medication whereas retrospective memory is needed to help the patient remember a dose has already been taken. When prescribed an antibiotic or other short-term prescription drug, most of us have experienced one or both kinds of memory failure: prospective (Oops, I forgot to take my pill this morning!) as well as retrospective (Did I take that pill or not?) The failure of our memory on such occasions, even when we have only one medication to take for days to a few weeks, gives us a good appreciation for what it must be like trying to manage five or more chronically administered medications.

Because central nervous system depressants such as alcohol can affect cognitive performance, it would not be surprising to learn that patients who regularly consume alcohol forget to take their medications. It is also possible that the health risk behaviors associated with substance abuse have a deleterious effect on attitudes regarding strict medication adherence. Cook et al.³ confirmed the association between problem drinking and decreased medication adherence among HIV-infected patients. Of note, most of the adherence problems among problem drinkers were related not to missing a dose but to simply taking a medication off cycle. While the authors state that "taking medications off schedule may result in the development of viral resistance," the evidence they cite is actually a small case series where days of medication were missed, rather than a dose taken off schedule.¹⁶ Nonetheless, the conclusion that attention to problem drinking is warranted makes good clinical sense, not only to improve medication adherence but also to reduce other alcohol-related complications.

Efforts are needed not to just reduce medications, but to reduce the use of inappropriate medications and increase the use of appropriate medications. Important outcomes include health-related quality of life, reductions in acute exacerbations of chronic diseases, and the cost-effectiveness of interventions. Further, assessment of patients' perspectives of these interventions should not be ignored. On one hand, patients appreciate the out-of-pocket cost savings of discontinuing unnecessary medications. On the other, patients perceive the need for their medications differently than physicians and often hold sacred their use of medications such as stool softeners that clinicians might dismiss as trivial. Lack of understanding of patient preferences can interfere with good doctor-patient communication, which is important for optimal medication adherence.

In summary, the studies reported in this issue show that provider feedback regarding a patient's medications on hospital admission, better methods of reconciling a patient's precise medication regimen, and improved recognition and management of comorbid substance abuse may all be small steps on the long road to reducing polypharmacy and improving adherence. As has been repeatedly shown for the optimal management of many chronic disorders, no single intervention is likely to be a complete solution, but rather needs to be integrated into a multicomponent systems intervention. Like chronic disorders, polypharmacy and medication adherence are complex phenomena that must be monitored in an ongoing and longitudinal fashion.¹⁷ A team approach that coordinates the roles of patients, physicians, nurses, pharmacists, allied health care personnel, pharmacy benefit managers, and payers is likely to be far superior to the disjointed efforts of individual parties. —**MICHAEL D. MURRAY, PHARM D, MPH**, *Department of Pharmacy Practice, Purdue University School of Pharmacy, Regenstrief Institute for Health Care, Indianapolis, Ind.*, and **KURT KROENKE, MD**, *Regenstrief Institute for Health Care, Indianapolis Ind.*, and *Department of Medicine, Indiana University School of Medicine, Bloomington, Ind.*

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