

Improving Medication Use for Older Adults: An Integrated Research Agenda

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Effective health care is a core determinant of successful aging, and medications are one of the most important therapeutic tools of health care providers. Most older adults use at least one prescription drug. Costs for these drugs are a substantial out-of-pocket expense for Medicare beneficiaries, and low-income older adults must weigh these costs against those of other basic needs. Although medications bring welcome relief to millions of elderly persons with age-related conditions, adverse drug events are an important cause of illness and death in these patients. Thus, the appropriate, cost-effective use of medication is central to successful aging.

Despite increasing attention to geriatric pharmacotherapy, there is an enormous need for additional research to improve the use of medications among older adults. The necessary research agenda encompasses much more than just the discovery of new drugs; better use of the current pharmacopeia has great potential

to improve the lives of older adults. We review four domains of pharmaceutical research: drug discovery and delivery, drug efficacy and safety, pharmacoepidemiology and drug policy, and improved access to and use of drugs. These domains encompass both the pre- and postmarketing phases of drug research. Premarketing research currently has greater magnitude and a better infrastructure than postmarketing research, yet issues arising in the two phases of research are equally important to the health and safety of older adults. A national, federally supported pharmaceutical database could greatly enhance the infrastructure of postmarketing research. However, many major improvements in medication use among older adults will also depend on closing the gap between knowledge and practice and increasing the ability of older adults to manage their medications.

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Ensuring appropriate and cost-effective drug use will be an important component of the agenda for future research on successful aging. Because they increase survival and improve quality of life, medications are among the most widely used and highly valued interventions for diseases of older adults. At least 85% of senior citizens use one prescription medication, and most use more than one (1). In 2002, more than 3 billion prescriptions were filled in the United States at a total cost of \$183 billion, an increase of 11% from 2001 (2). Millions of older adults also use nonprescription medications and herbal therapies, which can increase the risk for adverse drug interactions and events. The use and costs of medications will probably continue to increase, driven by growing numbers of older adults with chronic diseases amenable to pharmacotherapy (3).

The scope of pharmaceutical research necessary to promote successful aging will need to be considerably broader than a simple focus on new drugs. Although some research must center on the search for more effective and safer drugs, there is also a tremendous need for more research on improving the use of currently available medications. In this paper, we describe the landscape of pharmaceutical research and suggest areas of research that merit greater attention in the national quest to improve the lives of older adults. We focus on four core domains of pharmaceutical research, encompassing both the pre- and postmarketing phases of research.

THE PREMARKETING PHASE

Drug Discovery and Delivery

One important focus of pharmaceutical research is the development of better drugs and delivery systems. The

search for new chemical entities by medicinal chemists in both the public and private sectors drives the discovery of new drugs. These drugs are initially tested in animals, and promising agents undergo three phases of testing in humans before they are put on the market. Only one in five new drug applications results in a marketable drug product. Among marketable drugs, decisions about forms (for example, tablet, capsule, parenteral, or patch delivery systems) must be made with older adults in mind. Pill size, color, shape, and delivery system may each play a role in adherence. For example, intranasal administration of influenza vaccines may increase patient participation in immunization programs, and transdermal selegiline was recently found to be safer than selegiline administered in pill form (4). Drug discovery is fueled both by health care needs and by economic incentives in the pharmaceutical industry. Research and development dollars for new-drug discovery exceeded \$32 billion in 2002 (5).

Drug Efficacy and Safety

Pharmacokinetics and pharmacodynamics are key components of clinical pharmacology. For newly marketed drugs, research on disposition and action in older adults now derives from premarketing studies required by the U.S. Food and Drug Administration (FDA). Before 1990, however, few older adults participated in the premarketing phases of human studies. Little was learned about a drug's effectiveness and problems in elders until the drug reached the market and was used by many older adults. In August 1997, the FDA published guidelines encouraging the inclusion of elderly participants in trials of drugs likely to be used to treat diseases prevalent in older patients. This led to improved labeling instructions to help guide therapeutic

decisions, such as those on appropriate dosages for geriatric patients, and a “Geriatric Use Subsection” that contained further information specific to use of drugs in the elderly. This federal regulation provided important prescribing information to those caring for elderly patients. However, prescribing information alone is insufficient to ensure the appropriate use of drugs in clinical practice. Physicians may need information support when making prescribing decisions that take into account individual patient variables, such as current use of other prescribed drugs, renal function, cognitive function, and other factors important in judging the risk–benefit ratio of a medication (6).

THE POSTMARKETING PHASE

Pharmacoepidemiology and Drug Policy

Premarketing studies often include too few older participants to show important adverse effects of a drug in the elderly (7). Thus, the infrequent hazards of a medication generally become apparent only after the drug is prescribed for large populations (8). For this reason, observational studies are especially helpful in determining the relation between a medication’s effectiveness and its safety after marketing. Such studies require attention to important background characteristics of both patient and prescriber, some of which can be controlled by using statistical procedures, such as multivariable modeling or propensity scoring (9, 10). In practice, pharmacoepidemiology seeks to frame the benefits of medications against their potential harm in the heterogeneous population of older adults who are prescribed the drug. The United States has been slow to create the infrastructure needed to support these studies at a national level. Yet other countries have vigorously begun initiating such infrastructures (11).

Adverse drug events are a common form of preventable iatrogenic injury among older adults in all care settings (6, 12). Research suggests that this is due more to the number of drugs used by geriatric patients than to the effects of aging (13). Drug-related complications are two-fold greater in the elderly than in younger adults (12). Gurwitz and colleagues found that adverse drug events were common, often serious, and often preventable in ambulatory settings (6) and in nursing homes (14). Drug interactions are especially likely in elderly patients who use numerous prescription drugs coupled with self-administered interactants, such as over-the-counter and herbal remedies (15). Such interactions can cause harm or death and have resulted in the withdrawal of numerous drugs by pharmaceutical manufacturers (8). Collectively, these post-marketing studies emphasize the need for practices and interventions to reduce preventable errors of medication use, adverse drug events, and drug interactions. However, many adverse events result not from unknown effects of medications but from inappropriate prescribing. An assessment of the risks and benefits of a drug must take into

account the harm that may result from inappropriate prescribing.

The benefits and risks of drug products determine their value in practice and on the market. This value is relative to that of other drugs or treatments available for the same condition (16). Pharmacoeconomics research assigns this value as an aid in the development of drug policy. This research should focus on head-to-head comparisons of new and current medications commonly used for the same disorder, with the goal of identifying the most cost-effective drug. In some cases, a new, expensive drug may not be the most cost-effective (17). In other situations, although a new drug is more expensive, its overall costs may be lower if it reduces health care use; for example, if it decreases the number of hospital admissions (18). However, policymakers rarely have access to unbiased data on these topics because we lack a national infrastructure to oversee and mandate the investigations that produce such data. Thus, drug-benefit programs must often make decisions based on drug costs alone.

Improving Access to and Use of Drugs

The growing costs of pharmaceuticals have spurred employers’ drug-benefit programs to implement drug-management efforts, including promotion of the use of generic drugs, tiered copayment programs, and capped benefit programs. Although these efforts have helped reduce costs, they have done little to reduce out-of-pocket expenses for older adults, for whom out-of-pocket expenses have been especially high (19). However, an undue emphasis on drug cost alone may be harmful in some circumstances (20).

One proposed solution to high out-of-pocket costs for older persons is a national prescription plan. The costs of such a program are, of course, a major focus of debate. The U.S. government’s largest drug-benefit program, Medicaid, provides prescription coverage for 11% of poor persons in the United States (21). Older adults without Medicaid often lack the resources to pay for their medications, and poor, elderly members of groups without adequate prescription coverage have suffered disproportionately because of insufficient prescription coverage (22, 23). Most elders who can pay for their prescriptions have fixed incomes and therefore increasingly lose discretionary money as costs increase (24). On the basis of these findings, drug policy proponents recommend broad drug coverage within Medicare, especially for vulnerable persons (25). However, demonstrating cost-effectiveness and improving access to medications does not ensure appropriate prescribing.

Enormous gaps still exist between knowledge and prescribing practice. For example, even though unequivocal evidence from long-term effectiveness studies shows that control of hypertension reduces morbidity and mortality, only a minority of older adults with hypertension have adequately controlled blood pressures (26). The gaps are due to patient, physician, and healthcare system factors.

Patient factors include poor adherence to complex drug regimens; low tolerance of side effects; and the inability to prioritize long-term health outcomes (including survival) over more proximate issues, such as avoidance of nuisance side effects or competing financial demands. Physician factors include incomplete acceptance of recommended standards of care, competing clinical demands, and barriers to effective communication with patients about the health benefits of adherence (27). System factors include lack of access to health care, high medication costs, poor longitudinal tracking data on medication use, and complicated formularies.

Studies to improve prescribing for older adults are especially important with respect to drug safety, but underuse of potentially effective medications is also a problem. Some drugs are nearly always inappropriate for older adults because safer alternatives are available. Many studies (28, 29) have framed the need for better prescribing practices in all settings caring for the elderly. Early studies reported that one in five elderly patients receive an inappropriate drug or dosage (28). Recent studies suggest that clinicians continue to prescribe potentially harmful drugs (29). While the prescribing of inappropriate drugs or dosages is a major problem for older adults, some drugs are underused in these patients; these include warfarin for atrial fibrillation (30), statins for primary prevention of cardiovascular events (31), and angiotensin-converting enzyme inhibitors and β -adrenergic antagonists for cardiovascular disease (32, 33).

Decision support through informatics has been suggested as a core component of the infrastructure to improve medication use (34–37). Computer prescribing facilitates consideration of a vast array of detailed information ranging from drug and dosage selection to prevention of drug interactions and allergic reactions to medications. Many errors and adverse drug events can be prevented through computer-based information support (37, 38). Expert computer systems can rectify many prescribing and monitoring problems; for example, they can offer dosage adjustments based on a patient's renal function (39). A major question is whether such process improvements will improve relevant health outcomes (40).

Even when physicians prescribe appropriately, poor adherence is a major reason for therapeutic failure. Poor adherence can be due to incomplete engagement of patients in their care, polypharmacy, or prohibitive costs (41, 42). Patients may also complicate their prescribed treatment regimen with over-the-counter drugs; herbal remedies; and dietary supplements, such as vitamins (15, 43). Some of these complementary treatments can interfere with a prescribed regimen or can be harmful (44). Physicians may not know that patients are using these treatments; many patients do not volunteer the information, and physicians often fail to ask (41, 45, 46). More research is needed to promote adherence and medication management in older adults (47).

INTEGRATION OF THE RESEARCH AGENDA TO PROMOTE SUCCESSFUL AGING

A balanced research agenda to improve medication use in older adults will require integration of the four research domains reviewed here—drug discovery and delivery, drug efficacy and safety, pharmacoepidemiology and drug policy, and improved access to and use of drugs—and increased collaboration among the scientific disciplines involved with these domains. For example, pharmaceutical scientists and health services researchers might identify how adherence to a prescribed regimen varies by medication form or package design. Pharmacists and physicians might derive a feasible, reliable way to inform physicians of all drug products (prescribed and over-the-counter) obtained by patients at their pharmacy. Health care organizations and economists might determine the costs associated with establishing and maintaining evidence-based treatment-guideline programs. Drug policy researchers and trialists might assess the feasibility of trials of drug policy programs compared with assessments of the natural course of policy changes. Overall, we have much to gain from an intermingling of clinician-scientists in these research domains. All of this research requires an infrastructure to better support a population database for medication use in older adults.

The premarketing phases of pharmaceutical research currently enjoy more attention and funding than the postmarketing phases. While a proprietary industry drives innovation in premarketing research, postmarketing research relies too heavily on an informal research network and a limited clinical-reporting system. One solution to this imbalance would be a postmarketing database specifically designed to give researchers and policymakers prospective, timely information on rates of medication use and the outcomes associated with this use. A national prescription-drug database would facilitate postmarketing surveillance of medication use and allow scientists to design and test specific interventions to improve prescribing. Such a database could be created from computerized retail pharmacy data, much of which is already available in a standardized format to facilitate reimbursement by benefit managers. Although such a database has been needed for years, the impetus for the many relevant organizations to develop it was lacking until recently. An archival database containing prescription and outcomes data is being discussed as an early warning sensor for potential terrorism or for geographic tracking of such events (for example, prescribing of ciprofloxacin for anthrax). Such a system, motivated by concern about national security, could also provide the initial impetus and infrastructure for postmarketing drug surveillance.

Perhaps the single most important way to improve prescribing for older adults is to improve provider–patient communication and provide increased time for this communication, so that older adults can become more adept at

self-care. Ultimately, it is the patient or family caregiver who must take responsibility for long-term medication management. To get answers to their questions, patients often need more time from physicians and pharmacists than is typically available, and with older patients the time needed can be substantial. Health-illiterate patients especially suffer and could use simpler, more digestible written information that follows a schema for instruction (48). Physician-physician communication is also a problem. Many of these problems could be solved by general system improvements recommended for primary care (49) and for the management of patients with chronic disease (50–52).

CONCLUSIONS

Older adults have a greater burden of chronic disease and consume more drug products than any other segment of the population. In addition to using prescribed medications, older adults use other products, including over-the-counter drugs; herbal remedies; and dietary supplements, such as vitamins and minerals, all of which are ubiquitous. The widespread availability of potent drugs often further complicates an already-complex drug regimen, and this can lead to poor adherence to prescribed medications, drug interactions, adverse effects, and high costs to patients and to society. Both prescription and nonprescription drugs result in important out-of-pocket expenses for older adults. Solving these problems with attention to health outcomes is central to improving the overall use of drugs in older adults and requires a broad research agenda that will be enriched by input from multidisciplinary teams of health professionals.

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