The crucial role played by medication use in the elderly is common knowledge in the worlds of health services research, clinical epidemiology, and geriatrics. It is now widely known that although persons over age sixty-five represent only about 13 percent of the population, they consume nearly one-third of all medications in the United States; that medications probably are the single most important health care technology in preventing illness, disability, and death in the geriatric population; that drugs represent one of the largest and fastest-rising out-of-pocket health care expenditures for the elderly; and that the old, because of their high drug usage rate, greater frequency of coexisting illnesses, and diminished physiological reserves, are at greater risk of experiencing adverse drug effects. Yet despite this knowledge, the use of drugs by the elderly and their clinical outcomes have not been prominent research or programmatic priorities for federal government, philanthropic, or corporate grantmakers. Beginning in the mid-1980s, The John A. Hartford Foundation began a grant-making program in the area of medication use and aging, out of an interest in enhancing the therapeutic effect of drugs used by this age group and in reducing the frequency and consequences of adverse drug events.

After a number of years of active support in this area, the foundation convened its Expert Panel on Medications and Aging. This panel brought together authorities in the disciplines of geriatrics, gerontology, epidemiology, health services research, public policy, and pharmacology. Its mandate was to provide a consensus report that would critically define the further work needed to make the use of medications by the elderly more effective. This essay represents a synthesis of the work of that panel. The positions and opinions expressed below are extracted from transcripts of the expert panel’s deliberations, a structured survey administered to panel members,
reviews of the relevant clinical and policy research, as well as supplementary statements by panel members. These recommendations are designed to define the current issues relating to medication use by the elderly; to guide future activities of health care policymakers, grantmakers, providers, and payers; and to inform researchers, clinicians, and patients themselves.

**Current Status Of The Field**

In beginning its work, the panel identified six aspects of the health care system relevant to medications and the elderly: (1) health of elderly patients; (2) professional training of physicians, nurses, and pharmacists; (3) continuing professional education; (4) health policy planning; (5) quality of life among older Americans; and (6) iatrogenic complications in the elderly. Medications were seen as being vitally relevant to each of these areas, yet the panel felt that such points of intersection have not received adequate research or policy attention.

The group considered the current level of activity in this area conducted in several key sectors in the United States. Both the pharmaceutical industry and the National Institutes of Health (NIH) support important basic or developmental research leading to the production of new drugs that benefit the elderly. However, the panel’s concern was not the development of new agents, but rather research or programs designed to improve the use of available drugs. In this regard, the panel found only minimal activity in this field by the governmental, philanthropic, or corporate groups evaluated.

Panel members noted that throughout NIH in the past decade there has been only a single request for applications issued on the topic of medications and aging: a small program on geriatric pharmacology conducted on a one-time basis by the National Institute on Aging in 1989, which resulted in the funding of about ten modest-size research projects. A one-time request for applications issued by the Agency for Health Care Policy and Research (AHCPR) in 1992 dealt with the effectiveness of pharmaceutical therapy in general but did not specifically address medication use in the elderly. AHCPR planned to launch a follow-up grants program to focus on medication use in long-term care facilities. However, this program was removed from the agency’s agenda.

The Department of Veterans Affairs (VA), which provides nearly a billion dollars annually in drug benefits to a patient population that is increasingly elderly, has acknowledged the growing importance of geriatric pharmacotherapy to its mission and could become an increasingly active participant in this arena in the coming years. By contrast, NIH appears less committed to allocating resources to the study of therapeutic decision making and outcomes in the elderly at the population level. This problem
appears to be at least as acute at the National Institute on Aging.

As for the corporate sector, nearly all research funded by the pharmaceutical industry understandably is driven by the need to discover or promote specific products of a given company. However, support available from industry drops off sharply for the study of adverse effects of drugs in the elderly. If a proposed research project or intervention is unlikely to improve the marketability of a patented drug, chances of the work being funded are reduced further. One important exception has been Merck and Company, which has supported fellowship training in geriatric clinical pharmacology since 1988.

In the philanthropic sector, only the Hartford foundation has identified medication use by the elderly as a priority area for grant making. To our knowledge, no other foundation plans to move in this direction.¹

The panel spent considerable time examining areas where future activity could yield promising results in improving use of medications by the elderly. The group identified eleven priority areas, discussed below.

### Drug Testing, Development, And Labeling

**Gaps in the science base.** Most panel members agreed with the conventional wisdom that the elderly are more susceptible to adverse drug effects than are the young and may respond differently in terms of drug efficacy as well. However, it was noted that little information is available to define the separate effect of old age itself versus the comorbidity that often accompanies it. The panel believed that there is a dearth of solid pharmacological and epidemiologic data on these issues. This results in part from a perverse circularity: The very old (particularly the frail elderly) still are not well represented in premarketing studies of drugs, so that inadequate amounts of data are generated about such populations in clinical trials. Skepticism still exists at the Food and Drug Administration (FDA) concerning the magnitude and importance of differences in drug efficacy or toxicity that result from chronological age alone; this skepticism seems to result mostly from the absence of clear data demonstrating such age-related changes. In 1983 the FDA issued a Discussion Paper designed to focus attention on this area; the paper’s contents were issued as nonbinding recommendations in 1989.²

FDA and pharmaceutical industry representatives on the panel reported that the number of older patients being included in premarketing studies of drugs is growing. However, data indicated that often these patients are in their late sixties and early seventies and in good health, but that there are still relatively few patients over age seventy-five or with significant comorbidity. Thus, the relevance of study findings to patients in their eighties or to those with multiple medical problems may be limited.
Proposed action steps, (1) Commission a small series of projects followed by a conference to better define the pharmacologic basis of age-related differences in pharmacokinetics, pharmacodynamics, efficacy, and adverse effects. This would help to distinguish those aspects of “conventional wisdom” that have clear clinical and policy relevance from those that are plausible but unfounded. (2) Collect more precise information on the actual rate of inclusion of patients in all older age groups (not simply “over age sixty-five”) in new drug applications brought before the FDA in the past decade. Particular attention should be paid to the rate of inclusion of patients over age seventy-five, as well as patients with typical comorbidity and concurrent drug therapies. (3) Based on the above, prepare updated guidelines for including elderly subjects in premarketing drug trials.

Enhanced recruitment of appropriate elderly subjects. Enrolling adequate numbers of older patients in new drug testing is difficult in part because of researchers’ lack of experience with inclusion of such patients. Thus, even when there is willingness to recruit older subjects, they are often underrepresented because of the perceived difficulty in their recruitment and its attendant higher cost per subject. In reviewing this area, the panel saw that while there were members firmly holding positions on both sides of the issue of involving more elderly patients in premarketing drug trials, data were insufficient to support either position. One area of uncertainty was the actual demographic composition of participants in premarketing drug studies and how this has changed in the past decade. A second area of controversy was the actual incremental cost of including more older patients in such trials. Some believed that including large numbers of older subjects would impose considerable additional economic burden on companies attempting to bring products to market, and that the additional knowledge so gained would need to be weighed carefully in relation to the increased regulatory and economic burden that would be imposed. Conversely, others argued that older patients may in many respects be easier and less costly to recruit into studies because of easier availability of retirees and ready access to older patients living in congregate settings. There was, however, consensus on the fact that no clear data exist to inform the development of rational policy in this difficult area.

Proposed action steps. (1) Calculate the incremental cost of recruiting an elderly subject compared with a nonelderly one for typical drug trials, and estimate the cost/benefit implications of including older subjects. (2) Convene a working group of representatives of the clinical research departments of pharmaceutical manufacturers, geriatricians, biostatisticians, and regulators to address the following issues: the most cost-effective means of identifying, recruiting, and retaining elderly subjects for phase III clinical drug trials; statistical issues associated with analyzing data on subjects with
life expectancies that are shorter and confounding characteristics more complex than those of younger subjects; and quantitative and regulatory approaches to address these problems. (3) Support the development of consortia of elderly subjects (to be drawn from academically affiliated long-term care facilities, the nursing home industry, or primary care practices) to work with pharmaceutical manufacturers to recruit more typical elderly patients to participate in drug trials. (4) Identify current clinical, organizational, legal, and ethical barriers to enrolling adequate numbers of typical elderly patients, and propose methods to overcome them.

**Better identification of outcomes.** Trials of new drugs often focus on careful measurement of a target therapeutic outcome (for example, blood pressure) but may pay inadequate attention to other outcomes that can be particularly relevant to the elderly (for example, effects on cognition, mood, or gait stability). This is particularly problematic for older patients in whom a drug’s adverse effects in organ systems other than those targeted may be more prominent than its therapeutic effect.

Proposed action steps. (1) Initiate a series of consensus-development activities (including conferences and literature reviews) to define geriatrically relevant outcomes that should be studied in trials of drugs in several common therapeutic categories. Prominent among these outcomes would be functional status measurements, such as effects on mood, memory, attention, mobility, and “quality of life.” (2) Pay particular attention to defining age-related changes in the relationship between intermediary outcomes (for example, blood pressure, serum lipids, or intraocular pressure) and actual clinical outcomes of concern in the elderly (for example, stroke, cardiovascular disease, and visual loss due to glaucoma). Even when reduction of such intermediary risk factors by drugs has resulted in improved clinical outcomes in younger subjects, the effectiveness of such therapy has often not been convincingly demonstrated in the elderly.

**Labeling of prescription medications.** Labeling refers to the federally required specification of indications, instructions for use, efficacy, dosing, and adverse reactions that must be published for all prescription drugs. Despite the high proportion of drug usage accounted for by the elderly, the approved labeling for many commonly used drugs does not adequately address this population. Paradoxically, the official instructions for using many drugs common in geriatric practice often contain more information on the use of a given drug in pregnant women, nursing mothers, and children than in geriatric practice. A set of proposed regulations on geriatric-specific labeling was circulated by the FDA in 1990 but was never made into a regulatory requirement. Controversy surrounding this issue relates to the dearth of pharmacologic data described above under the first priority area. Some have argued that there is no need to identify special aspects of
the use of a given drug “in the elderly” if separate sections of the instructions already have addressed use of that drug in such situations as renal failure, hepatic insufficiency, or drug interactions with other drugs. However, most panel members believed that proper prescribing for the elderly would be best served by a single section integrating these concepts under the heading “Use in the Elderly” whenever the availability of adequate data made it possible. It was acknowledged that generating and synthesizing such age-specific information would entail costs of their own. However, such costs likely would be small in relation to the total development and promotional expenditures for most drugs and would be warranted in view of the potential for improving medication use in the elderly.

Proposed action steps. (1) Mandate universal inclusion in drug labeling of specific considerations for prescribing an agent in older patients, if the drug is regularly used by older age groups. Initially, given the current limited state of knowledge and experience concerning drug effects in older patients, for many drugs this section would have to state, “Inadequate information is available concerning use of this drug in patients over age seventy.” However, within five years such information could be required of manufacturers by the FDA as a condition for continued registration of a drug. Particular attention also should be paid to the labeling of over-the-counter drugs commonly used by the elderly. (2) Transform the FDA’s nonbinding guidelines on inclusion of elderly persons in clinical trials into formal policy.

Improving Prescribing And Utilization

Information for professional schools and continuing education. Geriatrics is still minimal or absent in the curricula of many schools of medicine, nursing, and pharmacy; education in drug therapy decision making likewise is given limited treatment in most medical school curricula. As a result, most medical students and other health professionals receive little grounding in geriatric pharmacology, even though prescribing for the elderly may be their single most important therapeutic activity. While the battle for curriculum time is a major problem in this regard, in many institutions the problem is the lack of availability of good teaching materials. This is particularly the case in continuing education programs. Clinicians in practice are faced daily with challenges related to the use of medications in the elderly and could provide an eager audience for continuing education on this topic. The panel recognized that inclusion of any new material into an already crowded curriculum might necessitate the exclusion of other material, requiring a kind of educational “cost/benefit” trade-off. However, the group believed that proper use of medications in an aging society was of such importance that rational preparation of clinicians in this...
area could plausibly displace at least some of the time devoted to less central areas of the medical curriculum, particularly if geriatric pharmacology were taught efficiently.

Proposed action steps. (1) Develop and actively disseminate essential curricula in geriatric pharmacology for insertion into predegree programs for doctors, nurses, and pharmacists. (2) Create an ongoing source of geriatric drug information to support standard postgraduate programs as well as innovative educational outreach initiatives for clinicians in practice that would be conducted by universities, medical societies, or managed care organizations. (3) Encourage the inclusion of practice-relevant material on geriatric pharmacology in certification examinations for physicians, nurses, and pharmacists.

**Scientific and epidemiologic basis for geriatric drug utilization review.** Despite the proliferation of federally mandated and proprietary computer-driven drug utilization review programs, there is little rigorous evidence to demonstrate the impact of such programs on clinical outcomes or health care costs. Where such evaluation has been attempted, results have often failed to provide evidence of benefit. In addition, the decision rules on which such programs are based often are proprietary and thus not available for scrutiny by researchers, clinicians, or the public. When such rules have been inspected, some algorithms have proved to be clinically implausible, particularly for the elderly. Nonetheless, initial computer screening of prescriptions for appropriateness and cost-effectiveness, followed by review by a well-trained clinician, could hold considerable promise for improving the quality and economy of drug use in all age groups, particularly the old. Unfortunately, this technology has proliferated before careful groundwork has been laid for its development or critical evaluation.

Proposed action steps. (1) Define the predictive value of commonly used drug utilization review rules for the elderly. (2) Evaluate the adequacy of drug utilization review programs, their role in influencing the quality and economy of drug therapy for the elderly, and their impact on the use of other health care resources. (3) Initially by means of a consensus development conference, and later by relying on actual data, develop drug utilization review decision rules that are more geriatrically and epidemiologically appropriate than those now in use. (4) Evaluate computer-based feedback at the point of prescribing to inform physicians of the appropriateness of their drug choices. Such programs should be developed and rigorously evaluated for use in hospital, community, and long-term care settings. (5) Examine the clinical and economic outcomes—both favorable and unfavorable—of implementing drug utilization review programs.

**Impact of regulatory and reimbursement policies.** Several recent initiatives were designed to influence drug use in the elderly, including the
Omnibus Budget Reconciliation Act (OBRA) of 1987, which limited antipsychotic drug use in nursing homes; various attempts at cost containment implemented by state and private authorities; and OBRA 1990 legislation on patient counseling and drug utilization review. Such regulatory or economic interventions often are implemented without any plan to evaluate their impact on drug use, clinical outcomes, or expenditures. Haphazard application of previously untested interventions on a large scale would be illegal for the introduction of new drugs, although it is commonplace for health policy interventions. Standards of efficacy and harm similar to those applied to new drug applications should be extended to the implementation of new policy interventions as well.

Proposed action steps. (1) Document the positive and negative effects of regulatory interventions at federal, state, and institutional levels that are designed to improve medication use in the elderly, as well as formulary-driven drug regimen changes in the private sector. Such evaluations must take into account not just the effect of the policy on medication utilization, but also its impact on use of other health care resources, patients' clinical outcomes, and total cost. (2) Encourage the development and prospective application of evaluation plans prior to widespread implementation of public or private programs to influence prescribing, to identify which ones work, which do not, and which may be harmful to patients. (3) Foster collaboration between geriatric clinicians, researchers, and policymakers in both the public and private sectors to facilitate the rigorous evaluation of reimbursement and regulatory strategies for geriatric drug use.

Measuring The Effects Of Marketed Drugs

**Systematic postmarketing surveillance.** Because of low representation of very old and frail elderly in premarketing studies, epidemiologic surveillance of adverse effects in large populations at the postmarketing stage provides a very important opportunity for detecting effects not identified in premarketing testing. This would be the case even with ideal representation of the elderly prior to marketing, because some adverse effects occur rarely or only in the face of unusual combinations of drugs or therapies; thus, they are unlikely to be detected in drug testing prior to widespread use.

Fortunately, there already are a number of databases that can be used for such postmarketing surveillance. Prominent among these are claims databases based on the Medicaid programs of several states. Because Medicaid covers much nursing home care, these programs (and the databases describing utilization within them) are heavily enriched with frail elderly patients. Increasingly, as more older patients move into managed care settings, databases based on health maintenance organization (HMO) care also will
become efficient tools for pharmacoepidemiology in this age group. Depiction of medication use is usually quite complete and accurate in such databases, because they are the means through which a pharmacy is reimbursed for a given prescription that has been filled. However, diagnostic information for outpatient care is frequently missing or incomplete, a problem that will need to be addressed to enable such databases to fulfill their substantial promise. As more health care information is automated (particularly in managed care organizations), this important deficit may be remedied. However, to the extent that Medicaid programs subcontract more and more care to managed care organizations, it will be vital to preserve the unique person-specific description of medications received, as well as details of other health care use. Availability of such data from non-Medicaid sources also will help with the generalizability of such research to nonindigent populations.

Proposed action steps. Provide resources for ongoing, systematic epidemiologic surveillance of drug use in the elderly and use this resource to generate regular reports on patterns of utilization (overuse, underuse, and potential misuse); develop new information on the causes and frequency of adverse drug effects in this age group; and use such databases to monitor the consequences of such adverse events.

**Comparative information on benefits and risks of common drugs.** Federal regulations now require that a new drug be shown to be meaningfully superior to placebo, but there is no requirement for comparative testing of a new agent against commonly used similar drugs within its class. As a result, while all drugs approved are effective and relatively safe, the current system leaves the clinician with little systematic guidance concerning the relative advantage or disadvantage of a newly marketed drug compared with other drugs within its class. Prescribers, patients, and payers must be able to discriminate among similar drugs in terms of their risks, benefits, and price, particularly for the elderly, who may be more vulnerable to suboptimal choices in all three domains. Current legislation does not require the FDA to collect such information or require manufacturers to generate it prior to drug approval. However, a pluralistic system of payers presents opportunities for innovative means of generating such information: Payers could require such information in evaluating drugs for formulary inclusion or for determining reimbursement.

Proposed action steps. (1) Identify drug classes commonly used by the elderly for which inadequate information exists concerning comparative efficacy or side effects. (2) Engage in “consciousness raising” among payers responsible for elderly medication reimbursement (for example, HMOs, insurance companies, the VA, and state Medicaid programs) to demonstrate the savings and quality-of-care improvements that would occur with
availability of such comparative drug data. (3) Help these groups to form consortia to fund and/or conduct large-scale simplified trials to generate such information at reasonable cost in the context of normal clinical practice. (4) Propose economic incentives and disincentives related to drug reimbursement or patent life to encourage the pharmaceutical industry to conduct or support such comparative studies.

**Economic Issues**

**Data on cost-effectiveness of similar drugs.** The arguments made above about comparative efficacy and toxicity apply as well to the comparative study of cost-effectiveness of drugs. At a time of ongoing reassessment of drug benefits for the elderly covered through managed care, it is appropriate that such large expenditures be made in the most cost-effective manner. However, the most cost-effective drug in a class may not be the cheapest; all analyses of cost-effectiveness of medications must account for both the clinical and the economic consequences of multiple outcomes associated with use (or nonuse) of a drug. This is particularly important in the elderly, in whom clinical outcomes that may not be directly related to a drug’s therapeutic indication can have a major economic impact.

Cost-effectiveness analysis is still subject to bias or sensitivity to initial assumptions. Nonetheless, some consensus is emerging concerning methodologic standards in this field, and the effects of biases and assumptions often can be discerned if they are presented openly and modeled appropriately. However, the rapidly increasing use of cost-effectiveness analysis will need to be matched by a rapid increase in the sophistication of both practitioners and consumers of such analyses if this approach is to retain legitimacy in both the marketplace and academic circles. Even when such analyses are performed impeccably, their conclusions must be seen as relating to populations of patients, rather than constraining prescribing for individual patients regardless of idiosyncratic differences. Given the very high benefits, risks, and costs of medication use in the elderly, they could serve as an appropriate subgroup in which to develop a sound approach to these issues. Outlines for the proper conduct of cost-effectiveness analyses of drugs have been published recently to guide such efforts.

Proposed action steps. (1) Gather and disseminate data from the literature on cost-effectiveness of similar drugs commonly used in the elderly. (2) Calculate economic savings that could be realized from use of the most cost-effective agents when possible, and make such information available to physicians and formulary committees. (3) Work with payer consortia to integrate cost-effectiveness components into comparative drug analyses.

**Drug reimbursement linked to adequate data.** It would be impractical...
to disallow reimbursement for all drugs with inadequate information about their use in the elderly, because this would remove many important agents from the available pharmacopoeia. However, in coming years it will be possible to institute economic incentives for manufacturers to generate such data as described below.

*Proposed action* steps. (1) Formulate policy options for private and federal payers to restrict payment beyond a specific time after approval for drugs for which inadequate data exist on effects in the elderly; analyze the impact of widespread implementation of such policies. (2) Consider incentives (patent life extension, more rapid premarketing approval, and greater reimbursement through Medicaid drug benefit) for products with well-documented profiles of geriatric effects.

**Concluding Comments**

The panel's deliberations occurred at a time of enormous progress in the development of new products of biological research, as well as rapid changes in the infrastructure of the U.S. health care system. Underlying both is the inexorable increase in numbers of elderly (particularly the “oldest old”) and their growing impact on medical care throughout the industrialized world. As a result of this confluence of events, the conclusions and recommendations of the Expert Panel on Medications and Aging may provide a timely means of guiding research, policy, and practice in this key aspect of health care for the elderly.

Members of the Expert Panel on Medications and Aging included William Abrams, Thomas Jefferson University; Jerry Avorn (chair), Harvard Medical School; Maude Babington, American Society of Consultant Pharmacists; Murk Beers, Merck and Company; Tom Felda, Health Care Financing Administration; Judy Garrard, University of Minnesota; Richard Greene, Agency for Health Care Policy and Research; Robert Kane, University of Minnesota; Lawrence Klein, The Johns Hopkins University/Georgetown University; Eileen Leonard, Food and Drug Administration; Helene Lipton, University of California, San Francisco; Wayne Ray, Vanderbilt University; Louise Rodriguez, Department of Veterans Affairs; Carl Saltman, Harvard Medical School; David Schulke, staff of Ron Wyden, U.S. Congress; and Al Siu, New York State Department of Health.

**NOTES**

1. As the report of the Expert Panel on Medications and Aging was being finalized, the trustees of The John A. Hartford Foundation elected to terminate the foundation's program of support in this area.