Department of Health and Human Services

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INTRODUCTION

The Department of Health and Human Services (DHHS) is the principal U.S. government agency assigned to protect the health of all Americans and for providing essential human services for those unable to help themselves. The goals of the DHHS, according to the strategic plan for fiscal years 2001–2006,[1] include reducing the major threats to the health and productivity of all Americans, improving economic and social well-being, improving access to health services, improving the public health systems, and strengthening the nation's health science research productivity. The DHHS accomplishes this mission through more than 300 programs under the leadership of the Office of the Secretary. DHHS programs are administered through 11 operating divisions utilizing nearly 62,000 employees and a budget approaching $400 billion.[1]

BACKGROUND

Many of DHHS' divisions are managed by the Public Health Service's (PHS) commissioned officers with the assistance of civil service employees. The commissioned officers corps consists of pharmacists, physicians, dentists, nurses, and other health care professionals. These officers and employees engage in clinical care, medical research, and disease surveillance through the DHHS divisions. Before the formation of the commissioned corps, pharmacists were already serving the American population through the Marine Hospital Service, which cared for merchant seaman in large seaport cities.[2] The services of the PHS expanded beyond seaports when Congress discovered the poor health care and living conditions of Native Americans under the authority of the Department of Interior's Bureau of Indian Affairs. In 1954, Congress transferred the care of all Native Americans from the Department of the Interior to the Department of Health, Education, and Welfare. With the creation of the Department of Education through the signing of the Department of Education Organization Act in 1979, the current DHHS officially succeeded the Department of Health, Education, and Welfare.

Throughout history, the divisions of DHHS have influenced many aspects of pharmacy practice and continue to have an impact on it today. Pharmacy practice is influenced by legislation administered through the DHHS divisions, through the funding of grants to support health care for the underprivileged and through research and the funding of research to monitor and improve health services. Each division plays a unique role in providing and improving health care.

AGENCIES OF THE DHHS

National Institutes of Health (NIH)

Although now considered the premier medical research organization, NIH's roots began in 1887 as a one-room laboratory, known as the Hygienic Laboratory, on Staten Island, New York. The laboratory was opened under the direction of Surgeon General John Hamilton to study major epidemics of the nineteenth century, including cholera, yellow fever, Rocky Mountain spotted fever, and hookworm.[2] The importance of the Hygienic Laboratory's work prompted legislation to move it to Washington, DC. Finally, in 1930, the Ransdell Act created the NIH to replace the Hygienic Laboratory. NIH researchers continue to investigate the causes of and cures for the nation's most devastating diseases. Currently, the 17 separate health institutes of the NIH are focusing large amounts of its nearly $18 billion budget on cancer, Alzheimer's disease, diabetes, arthritis, and acquired immunodeficiency syndrome (AIDS).[3] Along with performing research, NIH also supports nearly 40,000 research programs nationwide.

Food and Drug Administration (FDA)

The FDA is responsible for assuring the safety of foods and cosmetics, along with the safety and efficacy of phar-

maceuticals, biological products, and medical devices.[4] This authority to monitor medications and foods was first granted by Congress with the Food and Drug Act in 1906.[5,6] Assuring compliance with this important act remains a key function of the FDA.

Since 1906, various amendments to the Food and Drug Act have greatly influenced the practice of Pharmacy. The Sherley Amendment of 1912 was the first legislation to regulate the labeling of medications. The amendment mandated a guarantee against adulteration and misbranding from manufacturers.

The Delaney Clause, named for Congressman James Delaney, remains an important part of the 1958 Food Additives Amendment and the 1960 Color Additive Amendments to the Food, Drug, and Cosmetic Act. The clause states that "no additive shall be deemed to be safe if it is found to induce cancer when ingested by man or animal"[5] at any dose. The clause also recognizes and accepts that evidence of carcinogenicity in animals is sufficient to correlate to a risk in man. Examples of the FDA invoking the Delaney Clause include the removal of cyclamates, aminotriazole, and DDT from human food. Modernization of the act, to allow for a negligible risk standard, rather than the current zero risk, is currently being pursued.

The Kefauver–Harris Amendments of 1962 gave the FDA control over prescription drug advertising. According to the amendment, all advertisements and printed matter issued by a manufacturer must include the medication name, strength, side effects, contraindications, and information on effectiveness. Another major change to the act was the requirement that all medications must be shown to be effective, as well as safe. After this amendment, all new drug applications submitted to the FDA must contain research proving the effectiveness of the product. At that time, control over investigational medications and the inspection of factories was also transferred to the FDA.

Another amendment to the Food, Drug, and Cosmetic Act is the Nutrition Labeling Health and Education Act (NLHEA) of 1990. NLHEA is intended to provide consumers with information to help maintain healthy dietary practices and to protect consumers from unfounded health claims. NLHEA provides information to consumers by requiring nutrition labeling on all foods and dietary supplements. These nutrition labels must include the serving size, and number of servings per package, along with the amount of calories, fat, saturated fat, cholesterol, sodium, carbohydrates, sugars, dietary fiber, and total protein per serving. NLHEA also ensures the validity of nutrition claims by reviewing research submitted by manufacturers to ensure the claim meets with significant scientific agreement.

Centers for Disease Control and Prevention (CDC)

The roots of the CDC, the agency responsible for protecting health, are traced back to World War II. At that time the Malaria Control in War Areas (MCWA) attempted to control the spread of malaria among servicemen, along with preventing the introduction of the disease into the civilian population.[2] After the war, the importance of continued monitoring of infectious diseases prompted the conversion of MCWA to the Communicable Disease Center in 1946, the predecessor of the modern CDC. Today, the CDC monitors disease trends, investigates outbreaks and health risks, fosters healthy environments, and implements illness prevention measures and standards. The research performed by the CDC is primarily field research, as compared with the laboratory research that is performed by the NIH. More than 7500 employees and $3 billion per year are necessary to accomplish these goals.

Indian Health Services (IHS)

Although federally funded health services for Native Americans began in the early 19th century, the Transfer Act of 1954 propelled Native American health toward its modern form. This law transferred responsibility for the health care of Native American and Alaska Natives to the PHS. Soon after the transfer the PHS was directed by Congress to conduct health surveys of Native American populations. The first study was the Trachoma Study. This study found a widespread trachoma epidemic, along with increased incidence of other infectious diseases, including tuberculosis, among this population. These results prompted moves to improve sanitary living conditions and expand the provision of health care available to Native Americans.

Another PHS survey, the Meriam Report, also pushed for advances in Native American health care. Among the Meriam Report findings were that 1 out of 10 Native Americans had tuberculosis and over one-third of all Native American deaths were children under 3 years of age. These findings prompted moves for stronger health program supervision with more qualified staff and the establishment of health clinics on Native American reservations.

The findings of all the PHS surveys led to the formation of the current Indian Health Services as the fed-

eral agency responsible for providing health services to Native American and Alaska Natives. These services are currently provided to nearly 1.5 million persons in more than 550 federally recognized tribes in 35 states[7] with the goal to assure that comprehensive, yet culturally acceptable, personal and health services are available and accessible. The IHS currently maintains 36 hospitals, 58 health centers, 4 school health centers, and 44 health stations. With the health care provided by the IHS, the Native American life expectancy has increased 12 years since 1973,[7] with decreased infant and maternal pneumonia and influenza, tuberculosis, and gastrointestinal mortality. Despite these advances, IHS continues to work to reduce deaths due to alcoholism, accidents, diabetes mellitus, homicide, and suicide. The rates of death due to these causes remain significantly higher in the Native American population than the rest of the U.S. population.

Health Resources and Services Administration (HRSA)

HRSA provides the leadership necessary to achieve integration of service delivery to meet the health needs of Americans. This is done through the provision of personnel, educational, physical, and financial resources. Part of HRSA's $4.8 billion budget funds more than 3000 health clinics to provide medical care to more than 9 million individuals in underserved communities each year. HRSA also administers the Migrant Health Program, which provides grants to communities to support culturally based medical services to migrant and seasonal farmworkers and their families.

Although HRSA administers many diverse programs, one of the major programs is the Ryan White Comprehensive AIDS Resources Emergency (CARE) Act, Public Law 101-381.[8] The Ryan White CARE Act is named in memory of an Indiana teenager who increased awareness about the needs of people with AIDS while suffering from the disease himself. This act helps states, communities, and families to ease the burden of the AIDS epidemic. HRSA estimates 500,000 individuals with HIV and AIDS receive assistance through this act each year.[9]

The Ryan White CARE Act is divided into multiple parts with each part providing support to different segment of the AIDS community. The first part of the CARE Act, Title 1, provides grants to cities and large numbers of low-income, underinsured, or uninsured individuals with HIV and AIDS. These grants are intended to provide outpatient health care, prescription medications, home health services, hospice care, counseling services, and housing and transportation assistance. Title 2 of the CARE Act provides grants to states, Washington, DC, Puerto Rico, and other United States territories to provide health care to individuals living with HIV and AIDS. Title 2 is aimed at prolonging life and preventing hospitalization, particularly through assistance with obtaining medications through the AIDS Drug Assistance Program. With more than $150 million in funding from the CARE Act, the AIDS Drug Assistance Program allows states to establish programs to purchase and distribute antiretroviral therapy for low-income individuals. The third section of the act, Title 3, provides funds to public and nonprofit organizations to support early intervention services for low-income, medically underserved people at risk for HIV. These services are designed to slow the spread of HIV through education, counseling, testing, and early treatment. Title 4 provides grants to establish services for children, women, and families. In 1996, Part F was added to the CARE Act to combine other existing AIDS programs under the HRSA umbrella. Included in Part F are AIDS Education and Training Centers that train health care providers about the necessity of early intervention and appropriate treatment, Dental Reimbursement Programs that provide grants to dental schools to assist in covering costs incurred in providing treatment to HIV patients, and the Special Projects of National Significance Program that provides grants to develop models for providing care to persons with HIV in special populations.

Substance Abuse and Mental Health Services Administration (SAMHSA)

Although the Narcotics Division of the PHS (later renamed the Mental Hygiene Division) was created in 1929 to treat and study addiction, the National Mental Health Act of 1946 was the first legislation to authorize research and aid for mental health services. Starting in 1973, this act was administered by the Alcohol, Drug Abuse and Mental Health Administration (ADAMHA) through the National Institute of Mental Health (NIMH), the National Institute of Alcohol and Abuse and Alcoholism, and the National Institute on Drug Abuse. The current SAMHSA did not replace ADAMHA until 1992. SAMHSA continues ADAMHA's work to improve the quality and availability of substance abuse prevention, addiction treatment, and mental health services. The goal of SAMHSA is to reduce illness, disability, and death, along with the cost to society, which result from substance abuse and mental illness. SAMHSA is able to

provide federal grants to states to support programs intended to eliminate the stigma associated with substance abuse and mental illness, to disseminate information to improve available services, and to develop standards for the treatment of addicted and mentally ill persons.

Agency for Toxic Substances and Disease Registry (ATSDR)

ATSDR, one of DHHS' newest agencies, works to prevent exposure to hazardous substances from waste sites. The agency develops toxicological profiles of hazardous chemicals found at waste sites on the U.S. Environmental Protection Agency's National Priorities List. Its 400 employees also provide health education training in communities near these waste sites.

Agency for Healthcare Research and Quality (AHRQ)

Since its establishment in 1989, AHRQ has sponsored and conducted research to improve the quality of health care, reduce its cost, and increase access. It also supports research to address patient safety issues and medication errors. AHRQ's goal is to provide information that allows people to make better decisions about healthcare.

HUMAN SERVICES OPERATING DIVISIONS

Centers for Medicare and Medicaid Services (CMS)

The primary responsibilities of CMS, formerly known as Health Care Financing Administration (HCFA), include administration of Medicare and Medicaid programs. Since 1965, Medicaid has provided health coverage for low-income persons, while Medicare has provided for the elderly and disabled. Medicaid currently provides coverage for more than 34 million people, including nearly 18 million children. Medicare currently provides coverage for more than 39 million elderly and disabled Americans.[10] CMS requires a budget of $325.4 billion to provide these and other services. Among CMS other responsibilities is administration of the Children's Health Insurance Program. The Children's Health Insurance Program provides reduced or no-cost health coverage for more than 2 million children under the age of 19 whose families earn too much to be eligible for Medicaid but do not earn enough to afford private insurance.

Administration for Children and Families (ACF)

The ACF, established in 1991, maintains more than 60 programs that promote the economic and social well-being of children, families, and communities. Many of ACF's programs are aimed at helping children, with the most widely recognized being the Head Start Program. Head Start works with children from birth to 5 years of age, pregnant women, and their families to increase the school readiness of children from low-income families. ACF also funds programs to prevent child abuse and domestic violence. ACF continues to administer a national enforcement system that works to collect child support payments from noncustodial parents.

Administration on Aging (AoA)

Establishment of the AoA was mandated as part of the Older Americans Act of 1965. The Older Americans Act was passed as a means to organize, coordinate, and provide community-based services and opportunities for older Americans and their families. Although AoA programs are available to all Americans 60 years of age or older, priority is given to those with the greatest need. AoA's work is intended to protect the rights of vulnerable and at-risk persons, educate the community about the danger of elder abuse, and provide employment opportunities for older Americans.

Office of the Secretary of Health and Human Services (OS)

The Office of the Secretary provides leadership for the entire DHHS. It is responsible for advising the President on issues relating to health and welfare. The most recent expansion in the OS is the formation of the Office of Public Health Preparedness (OPHP) in late 2001. This office was created in response to the terrorist attacks on September 11, 2001. The OPHP directs the DHHS' activities aimed at protecting the population from acts of bioterrorism and other public health emergencies. Working with the Office of Homeland Security, OPHP's efforts are aimed at coordinating the preparation for and recovery from such events.

Program Support Center (PSC)

The final DHHS agency, PSC, provides administrative support for the DHHS. PSC is a self-supporting division that operates as a business-like enterprise. Their mission

is to provide "qualitative and responsive 'support services' on a cost-effective, competitive, 'service-for-fee' basis";[11] to DHHS agencies and other federal agencies. Services available through PSC include personnel, grants, information technology, and administrative services.

Through the many divisions of the DHHS, the pharmacists of the PHS have worked to improve and protect the health of Americans, particularly those who are unable to care for themselves. Not only do pharmacists play an important role in the DHHS, but the DHHS influences pharmacist on a daily basis. Pharmacy practice is continually influenced by legislation administered through the DHHS divisions, through the funding of grants to support health care for the underprivileged and through research and the funding of research to monitor and improve health services.

The DHHS influence is apparent on every medication bottle delivered from the manufacturer, in the patient counseling techniques utilized, and treatment guidelines and research protocols administered throughout the country.

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10. HCFA: Health Care Financing Administration. www.hcfa.gov. September 2000.
11. Program Support Center. http://www.psc.gov/concept.html (accessed September 2000).

PROFESSIONAL DEVELOPMENT

Diabetes Care, Pharmacy Practice in

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INTRODUCTION

When people talk about pharmacy practice in diabetes care, the first thought that comes to most peoples' minds is the community pharmacist dispensing a prescription for a blood glucose lowering medication. However, pharmacists are involved at a much deeper level in the care of patients with diabetes. In this article, examples of different ways pharmacists are involved in the care of patients with diabetes are provided. Resources to learn more about diabetes, as well as tools that will assist you in providing care, are also indicated.

COMMUNITY PHARMACY

Diabetes services in community pharmacies range from basic to complex. Basic services include the following:

1. The dispensing of medications and counseling about their proper use, storage, side effects, and potential drug interactions is the minimal involvement that pharmacists in this setting should have.
2. Educating patients about the proper use of ketone strips, lancing devices, and the proper selection of over-the-counter (OTC) products is included as a basic service.
3. Pharmacists may want to devote a section of the pharmacy, or at least shelf space, to specific products for patients with diabetes, or to enroll in one of the franchises that sells these products to pharmacies to help them with marketing and signage.
4. Patient education flyers, pamphlets, and video tapes may be ways that pharmacists try to improve the knowledge of their customers with diabetes.

More in-depth services include the following:

1. Educating patients about the proper use of blood glucose monitoring products and discussing before and after meal blood glucose target ranges and helping patients to determine causes of above and below target range readings requires more time.
2. Holding blood sugar screening programs in a store to increase diabetes awareness and potentially identify undiagnosed patients. This can be performed by the pharmacist or in conjunction with a local diabetes education program.
3. Performing talks for civic and diabetes support groups is a way to let people know that there is a pharmacist that is knowledgeable about diabetes in their community.
4. Having diabetes days in the pharmacy where different local diabetes educators and health professionals discuss or perform services in the store.
5. Fitting and selling orthotic shoes.
6. Many pharmacists, especially those who own their own stores, have turned to compounding as a means for financial and professional satisfaction. Compounding topical products for peripheral neuropathy, wounds, periodontal, and retinopathy are a few examples.

Complex services include the following:

1. Develop and run a diabetes education/management program through a pharmacy. This can be performed on a basic level where patient assessment to identify areas that the patient needs education in and performance of certain educational components occurs in the pharmacy. Components that the pharmacist may perform for this level of service are medication review, discussion of the differences in Type 1 and Type 2 diabetes, reasons that the person or family member developed diabetes, signs/symptoms, causes and treatments of hyperglycemia and hypoglycemia, basic foot screen, and reminder and education about tests that should be performed and their frequency. Areas such as nutrition counseling, foot care, and medication adjustments are referred to other providers.
2. Pharmacists that are more comfortable with their diabetes knowledge and counseling skills may per-

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form basic nutrition assessments, or educate patients on carbohydrate counting and the exchange systems of meal planning. They may discuss medication adjustments, specifically increases or decreases in insulin dosage, based on blood glucose readings and the carbohydrate content of the next meal. In-depth discussions about the cause, prevention, and treatment of complications of diabetes may be part of the education provided to patients. Pharmacists may provide these services by themselves or hire a nurse or dietitian to work with them through the pharmacy. The creation of educational rooms where individual and group sessions can occur are often created to give the pharmacist, educators, and patients privacy. By having a nurse and dietitians on staff as part- or full-time employees, pharmacists can apply to become American Diabetes Association Recognized Outpatient Education Providers and to be subsequently reimbursed by medicare for their educational services.

HOSPITAL PHARMACY

Pharmacists can provide diabetes care in the hospital setting in several ways. One way is to perform in-services to the nursing and hospital staff on medication used in treating diabetes and comorbidities. Which blood pressure medication should be used in patients with microalbuminuria, and why? Which medications when used in patients with diabetes can cause an increase or decrease in blood sugar levels? What contraindications should they look out for in patients in the hospital with diabetes? Another way is to actively participate in patient education of inpatients or outpatients.

In most instances, pharmacists are relegated to the medication or blood glucose monitor counseling aspect only. In some hospital programs, pharmacists are the diabetes coordinators and perform all areas of administration and patient education. Preparing IVs for patients with diabetes undergoing surgery, those admitted with diabetic ketoacidosis (DKA), or newly diagnosed patients are common areas of pharmacist involvement in hospitals.

CLINICS

Pharmacists may be involved in a variety of clinics. Armed forces clinics or specialty clinics that are part of hospitals are the largest types of freestanding clinic for patients with diabetes. Pharmacists are involved with the dispensing, medication counseling, and to some degree, counseling about some aspect of diabetes. Clinics for indigent patients are becoming more common with the number of working poor increasing. Pharmacists may be involved with collaborative practice arrangements with physicians where medication changes are made based on the pharmacist assessment in some cases. This type of setting tends to give the pharmacist flexibility to perform diabetes education and management services.

PHYSICIANS' OFFICES

Physicians are being overburdened by patient visits and the necessity to follow the Health Plan Employer Data and Information Set (HEDIS) and other practice guidelines. Pharmacists can perform chart reviews to see if patients with diabetes have received regularly scheduled test for A1C, urinary microalbumin, lipid measurements, referral for dilated eye exams, foot assessment and foot care, and blood pressure measurements.

Pharmacists can assist the physician by assessing clinical outcomes of diabetes, hypertension, thyroid disorders, and lipids, and making recommendations to the physician about the potential need for adjustments in medications. Pharmacists can also educate individuals and groups of the physician's patients on diabetes within the office setting.

PRIVATE PRACTICE

Some pharmacists are confident in their counseling and business skills to where they develop their own private practice. However, in the United States, this is not common for pharmacists to do and heavily relies on individual state's reimbursement for diabetes education and management services. Services are provided in clinic-type settings, in other pharmacist's practices, and even over the Internet and phone. This area will expand when reimbursement improves for the provision of these services. Examples of a few of these services are The Diabetes Center in Connecticut, and Diabetes In Control, which is an Internet business.

NURSING HOMES AND ASSISTED LIVING FACILITIES

Type 2 diabetes is common in the elderly. Most nursing home and assisted living facilities are staffed by Certified Nursing Assistants. These staff need to be trained in the proper care of patients with diabetes. Training on the

identification of the signs/symptoms, causes, and treatments of high and low blood glucose is a basic training skill that all staff should know, but few do. A written protocol should be available and accessible to staff. In-services, including medications, blood sugar reading assessments, and foot and skin care, should be covered quarterly with staff and even more frequently in some homes due to the high turnover rate of staff. It should be included in all new hire training.

PHARMACEUTICAL INDUSTRY AND DIABETES PRODUCT SALES

Pharmacists that work for pharmaceutical companies may be involved in diabetes care either as salesmen, clinical education consultants, or researchers. The number of products used in the treatment of diabetes is expanding as we learn more about the underlying causes of the disease. Since the late 1990s, more than five new oral agents and three new insulins have come into the marketplace. Pharmacists have played an integral part in educating physicians, other pharmacists, and other health care personnel on actions and uses of these new products. Clinical education consultants or medical liaisons for pharmaceutical companies take this education a step further by providing continuing education and clinical assistance to the physicians in the treatment of their patients with diabetes. It is evident with the development of the alpha glucosidase inhibitors, meglitinides, thiazolidinediones, and new insulin formulations such as lispro and glargine that researchers have been trying to develop products that improve the outcomes of these patients. The number of products used for patients to check their blood sugar has mushroomed since the early 1990s. Blood glucose monitor technology has allowed patients to perform these tests with minimal invasion. The development of truly noninvasive blood glucose monitoring; testing devices for home use for blood pressure, cholesterol, and A1c; and other diabetes-related devices will require sales personnel with more technical and medical knowledge that those used in the past.

MANAGED CARE AND PRESCRIPTION DRUG BENEFIT ADMINISTRATORS

With passage and implementation of national medicare prescription drug coverage, pharmacists will need to take a more active role in the development of reasonable, effective formularies of medications used to treat diabetes and the supplies necessary for patients to achieve optimal outcomes. Pharmacists working for managed care organizations may be in decision-making positions that determine the frequency and type of diabetes education that particular insurance companies will provide to their cardholders. Pharmacists that have been involved in diabetes care know of the importance of individual assessment and periodic follow-up to assess maintenance of optimal therapeutic and personal outcomes. Pharmacists without this background may only look at products and educational services as a current cost without taking long-term benefits into consideration.

Comprehensive diabetes management programs that have showed positive clinical and financial outcomes extend past the examples of the Asheville Pharmacy Project, the Mississippi Medicaid Project, and the South Carolina Pharmacists Diabetes Management Programs. The degree of reimbursement for diabetes education services often differs by state.

CONCLUSION

Pharmacists can be involved in a variety of areas of diabetes care. These areas can range from direct, with personal intervention and counseling, to indirect by deciding what services and products a patient may obtain. With any pharmacist practice, the environment, financial constraints, time limitations, desire, and competence of the pharmacist each play a role as to the involvement a pharmacist has with a person with diabetes. With the number of cases of diabetes expected to increase, pharmacists can and should play a more prominent role in assisting patients with diabetes.

Resources for information about diabetes products and management are abundant. Below are some of the many informative web sites available to patients and pharmacists that will enable them to increase their knowledge about diabetes.

DOCUMENTATION FORMS

Forms to document patient assessments and educational session content are abundant. Individual practices can modify these forms to meet their specific locations needs. Examples of these forms are often included in certificate programs such as those offered by the National Community Pharmacist Association, American Pharmaceutical Association, American Association of Diabetes Educators, and state pharmacy organizations. These forms are also found on the different web sites, such as www.bd.com, www.novo.dk, and www.humulinpen.com.

SOME DIABETES-RELATED WEB SITES

www.aadenet.org
www.pharminfo.com/disease/immun/#iddm
www.ezdiabetes.com/
www.afpafitness.com/FACTINDX.HTM
http://medicine.ucsf.edu/resources/guidelines/guidedm.html
www.pfizer.com/main.html
www.cdc.gov/diabetes/index.htm
www.diabetes.org/
www.avandia.com
www.actos.com/
www.novo.dk/health/dwk/info/ydww/index.asp
http://diabetes.lilly.com
www.eatright.org/
www.diabetesmonitor.com/tx_tin2/sld001.htm
www.joslin.harvard.edu/education/library/oha.html
www.lifescan.com
www.intelihealth.com/IH/ihtlH?t=21054
www.niddk.nih.gov/health/diabetes/diabetes.htm
www.cdc.gov/nccdphp/cdnr.htm
www.aace.com/indexnojava.htm
www.bms.com/products/index.html
www.aventispharma-us.com
www.aafp.org/acf/1999/resource.html
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Dietary Supplement Health and Education Act

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INTRODUCTION

President Clinton made history when he signed the Dietary Supplement Health and Education Act (DSHEA) into law in 1994. The DSHEA amended the Federal Food, Drug, and Cosmetic Act to create a new regulatory category of products: dietary supplements. The DSHEA exempts dietary supplements from laws regulating drugs, as long as the manufacturer does not claim that the supplement can diagnose, mitigate, treat, cure, or prevent disease. This monograph describes the history and provisions of the DSHEA, and its importance to pharmacists. This monograph will also compare the regulation of drugs and dietary supplements, address the minimal FDA scrutiny and inadequate safeguards required by the DSHEA, and the implications for pharmacists.[1,18,19]

HISTORY OF THE DSHEA

The Federal Food, Drug, and Cosmetic Act was passed in 1938 after the use of diethylene glycol as an ingredient in a sulfanilamide elixir resulted in the deaths of almost 100 people. This law empowered the FDA to require New Drug Applications (NDA) to have evidence of safety and efficacy from the manufacturer before a product could be marketed. Although the law intended more FDA regulation for dietary supplements than foods, the regulations promulgated by the FDA left unanswered questions about how products for "special dietary uses" should be classified and regulated. During the following decades, policy on dietary supplements was created largely through FDA litigation. In 1962, following public alarm at thalidomide-induced birth defects in Europe, Congress passed the Kefauver–Harris Act, which required drug manufacturers to provide scientific proof that a drug was safe and effective before marketing, and tightened control over products classified and sold as drugs.[4,5]

Following the passage of the Nutrition Labeling and Education Act in 1990 that granted additional labeling authority to the FDA, dietary supplements would be subject to stricter criteria for health claims under proposed new regulations. Congress also began deliberation on bills that would increase the FDA's enforcement powers and amend the Federal Trade Commission Act to prohibit advertising nutritional or therapeutic claims that were not on supplement labels. Fearing the impact of these pending regulations and laws, the health food industry mounted a massive grass-roots effort to limit FDA jurisdiction of dietary supplements. Additionally, heightened concerns about the escalating costs of traditional medicine and a cultural climate promoting self-care and healthy lifestyle fueled demand for greater access to self-treatment. Congress passed the Dietary Supplement Health and Education Act of 1994 citing improvement in the health status of U.S. citizens as a top government priority.[1,3,6,7]

ANATOMY OF THE DSHEA: INTRODUCTORY SECTIONS (SECTIONS 1–4)

The DSHEA contains 13 sections that define dietary supplements, set forth regulatory requirements, and provide for the administration of the DSHEA. The provisions of the DSHEA for regulation of dietary supplements are vastly different from the regulation of drugs (Table 1). The first and second sections include an overview and rationale for the DSHEA. Section 3 defines dietary supplement as a product intended to supplement the diet that contains one or more of the following ingredients: vitamins, minerals, herbs or other botanicals, amino acids, dietary substances intended to supplement the diet by increasing dietary intake, and any concentrate, metabolite, constituent, extract, or combination of any of these ingredients. Interestingly, the DSHEA does not require that the substance must provide dietary or nutritional benefit, despite the fact that it is intended to supplement the diet. The DSHEA specifies that a dietary supplement is for oral use in tablet, capsule, powder, softgel, gelcap, or liquid form. The DSHEA explicitly excludes tobacco, meal replacement products, and substances that have previously been approved as a new drug, antibiotic, or biologic. The DSHEA also specifically excludes dietary supplements from the definition of food additive, reversing prior re-

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Table 1 Comparison of dietary supplement versus drug regulation

Distinguishing feature	Dietary supplement	Drug
Description	Vitamins, herbs or other botanicals, minerals, amino acids, substances intended to supplement the diet	Substances approved by the FDA as prescription or nonprescription drugs
Route of administration	Oral	Oral, parenteral, topical
Safety standard	Reasonable expectation of safety	Reasonable certainty of safety
Safety data requirement	None required for any product sold before 1994 (most products) New dietary ingredients require safety data to be submitted to FDA prior to marketing	Submitted to FDA prior to marketing
Adulteration	Burden of proof on FDA	Burden of proof on manufacturer
Nutritional labeling	Required	Not required
Labeling	No FDA review required as long as labeling is not attached to product	FDA review required on all labeling prior to distribution
Indication	To treat a nutrient deficiency, to affect the structure or function of the body, to maintain well-being	To prevent, treat, cure, or diagnose disease or other pathologic conditions
Ingredient listing	No requirement that all ingredients, active and inert, be listed on product label. In multiingredient proprietary mixtures, quantities of individual ingredients are not required	All ingredients of active constituents must be listed with quantity. Inert ingredients must also be labeled
Good manufacturing practices	Standards set by industry groups or individual manufacturer (not yet established by FDA)	Set by FDA

(From Refs. [1,4,8,9].)

gulations and legal decisions by which the FDA had prohibited dietary supplements as unapproved food additives.[1,8,9]

Section 4 of the DSHEA establishes adulteration provisions for dietary supplements. The DSHEA sets considerably less stringent safety standards for dietary supplements than those required for drugs or food additives. The FDA safety standard for drugs and food additives is a "reasonable certainty" that a substance is not harmful. In contrast, the DSHEA requires a "reasonable expectation" of safety for dietary supplements. Manufacturers are not required to submit safety data *for most products* to the FDA prior to marketing dietary supplements; the product is presumed safe. The burden of proof to show that a dietary supplement is adulterated or unsafe is the responsibility of the FDA. Additionally, the DSHEA defines a dietary supplement as adulterated if an ingredient presents "a significant or unreasonable risk of illness or injury" when used as directed on the label. The adulteration definition for dietary supplements focuses on the *toxicity for a labeled use*, unlike standards for drugs and food additives which focus on the toxicity of product itself, regardless of labeled use. For example, a dietary supplement that is used as a substance of abuse cannot be removed from the market unless the FDA can prove that it is unsafe for its labeled use.[1,4,10]

ANATOMY OF THE DSHEA: MARKETING AND LABELING OF DIETARY SUPPLEMENTS (SECTIONS 5–7)

Section 5 of the DSHEA addresses dietary supplement claims and marketing. Unlike drugs for which any advertising, informational, or promotional material is considered labeling by law and is subject to FDA review before distribution, dietary supplement literature is not deemed labeling. "A publication, including an article, a chapter in a book, or an official abstract of a peer-reviewed scientific publication that appears in an article and was prepared by the author or editors of the publication, which is reprinted in its entirety" is not considered labeling under the provisions of the DSHEA. The DSHEA requires that the information presented must not be false or misleading, cannot promote a specific supplement brand, must be displayed with other similar materials to present a balanced view, must be displayed separate from supplements, and must not have other information at-

tached, such as product promotional information. The DSHEA relies on good faith marketing by the manufacturer to adhere to these requirements.[1,10,18,19]

Section 6 of the DSHEA amends the Nutrition Labeling and Education Act to allow four types of label claims on dietary supplements without obtaining premarketing approval by the FDA. A product may claim a benefit related to a classical nutrient deficiency, as long as the U.S. disease prevalence is disclosed. The label may also describe the role of a nutrient or dietary ingredient that is intended to affect the structure or function of the human body (so-called structure and function claim), or characterize the documented mechanism by which a nutrient or dietary ingredient acts to maintain such structure or function. The label may also include a statement about general well-being from consumption of a nutrient or dietary ingredient. If any of these claims is made, the product must also include the following statement: "This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease." It is the manufacturer's responsibility to substantiate these claims and submit the information to the FDA within 30 days after marketing, but, unlike requirements for drugs, FDA approval of claims is not required before marketing. The definition of what information is required to substantiate a claim is not addressed by the DSHEA.[1,11]

In subsequent rulemaking, the FDA clarified structure and function claims, which are widely used by supplement manufacturers. FDA rules prohibit specific disease claims, such as prevents osteoporosis and implied disease claims, such as prevents bone fragility in postmenopausal women, without prior FDA review. Express and implied disease claims are allowed through the name of the product, for example, "Carpaltum" or "CircuCure." The use of pictures, vignettes, or symbols, such as electrocardiogram tracings, is also permitted. Additionally, health maintenance claims, such as maintains a healthy circulatory system, and nondisease claims, such as for muscle enhancement or helps you relax, are allowed. The FDA also clarified structure and function claims to include for common, minor symptoms associated with life stages. For example, common symptoms of PMS or hot flashes are permissible structure and function claims.[1,11,18,19]

Section 7 of the DSHEA addresses dietary supplement ingredient labeling and nutrition information labeling. The label must identify the product as a dietary supplement. To avoid misbranding, supplement labels must include the name and quantity of each active ingredient. If the product is a proprietary blend, the total quantity of all ingredients in the blend (without listing quantities of individual ingredients) may be used. If the product contains botanical ingredients, the label must state the part of the plant used in the supplement. Listing of inert ingredients is not required. Supplements that claim to conform to the standards of an official compendium, such as the U.S. Pharmacopeia (USP) or National Formulary (NF), must meet the specifications of the compendium to avoid misbranding.[1,10,11]

Dietary supplement labels must also include nutrition labeling. Ingredients for which the FDA has established Reference Daily Intake (RDI) or Daily Reference Value (RDV) are listed first, followed by ingredients with no daily intake recommendations. If an ingredient is listed in the nutrition labeling, it does not have to be included again in the list of ingredients. Dietary ingredients that are not present in significant amounts do not need to be listed. Significant amounts are not defined by the DSHEA. The label must state a suggested quantity (dose) per serving.[1,10,11]

ANATOMY OF THE DSHEA: ADMINISTRATION (SECTIONS 8–13)

Section 8 of the DSHEA is a grandfathering clause. Substances in use prior to October 15, 1994 are not subject to the standard of reasonably expected to be safe. Substances marketed after this date are considered new dietary ingredients. Unless the dietary supplement was "present in the food supply as an article used for food in a form in which the food has not been chemically altered," the manufacturer must notify the FDA at least 75 days before marketing the product. The manufacturer must supply the FDA with information based on history of use or other evidence of safety to support that the product will reasonably be expected to be safe for the stated use. There are no guidelines in the DSHEA for what constitutes history of use or other evidence of safety.[1,8,9]

Section 9 gives the FDA the authority to establish good manufacturing practice (GMP) regulations to control the preparation, packing, and storage of dietary supplements. The DSHEA specifies that the GMP regulations for dietary supplements should be modeled after current GMP regulations for the food industry. To date, the FDA has not established GMP regulations for dietary supplements.[1,4,10]

The remaining four sections of the DSHEA are administrative provisions to implement and support the DSHEA. Sections 10 and 11 override prior legislative and regulatory actions that conflict with the DSHEA. Section 12 set up a Commission on Dietary Supplement Labels, which was composed of nutritionists, industry representatives, a pharmacognosist, and attorneys to make re-

Table 2 Recommended dietary supplement references for pharmacists

Pharmacist's Letter/Prescriber's Letter Natural Medicines Comprehensive Database, 4th ed., Jeff M. Jellin, Philip Gregory, Forrest Batz, and Kathy Hitchens, ed. Stockton, CA: Therapeutic Research Faculty, 2002. Also online at www.NaturalDatabase.com (updated daily).
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The Review of Natural Products. Ara DerMarderosian, ed. St. Louis, MO: Facts and Comparisons, Inc. (published monthly).
The Cochrane Library, 2002. Oxford: Update Software. Online at www.update-software.com (updated quarterly).
Herbal Medicine: Expanded Commission E Monographs. Mark Blumenthal, ed. Newton, MA: Integrative Medicine Communications, 2000.

commendations for dietary supplement label claims. The Commission submitted its findings to the president and Congress in 1997.[12]

The last section of DSHEA, Section 13, establishes an Office of Dietary Supplements (ODS) within the National Institutes of Health (NIH). The purpose of ODS is to conduct and coordinate scientific study within NIH relating to supplements in maintaining health and preventing disease and to collect and compile scientific research, including data from foreign sources and the NIH Office of Alternative Medicine. The OCS is also responsible for serving as the principal advisor to other government agencies on issues relating to dietary supplements, compiling a database on scientific research on dietary supplements and individual nutrients, and coordinating NIH funding relating to dietary supplements.[1,13]

The FDA Center for Food Safety and Applied Nutrition published a 10-year plan for fully implementing the DSHEA. The goal of the plan is, "By the year 2010, have a science-based regulatory program that fully implements the Dietary Supplement Health and Education Act of 1994, thereby providing consumers with a high level of confidence in the safety, composition, and labeling of dietary supplement products." In the plan, the FDA details strategy to improve safety and labeling; clarify structure and function claims, and differences among dietary supplements and foods and drugs; improve enforcement of the DSHEA provisions; enhance science and research capabilities; and improve communication with the public. Pharmacists should be familiar with the DSHEA and FDA rules concerning dietary supplement products to be effective conveyors of consumer information.[20]

IMPLICATIONS FOR PHARMACISTS

Dietary supplement sales have grown from $8.8 billion since the passage of the DSHEA in 1994 to a projected $15.7 billion in 2000. Nearly half of Americans surveyed report using vitamins, herbal products, or other supplements. The DSHEA exempts dietary supplements, most of which are nonpatentable, from the multimillion dollar FDA drug approval process and simultaneously shifts the burden of proof of safety from the manufacturer to the FDA. The DSHEA allows marketing of substances with safety standards that predate the Food, Drug, and Cosmetic Act of 1938.[2–4,11]

Pharmacists should be aware of the differences in safety standards and regulatory control between drugs and dietary supplements (Table 1). When counseling people about dietary products, pharmacists must be aware that the DSHEA allows the promotion of substances that may have variable potency, unidentified components, unproven efficacy, and unknown adverse effects. The DSHEA does not require warnings about drug interactions or medical conditions under which a dietary supplement should not be used. In view of the liberal labeling provisions of the DSHEA, pharmacists cannot trust dietary supplement company literature and should consult reliable information sources (Table 2).[1,17]

CONCLUSION

Although the passage of DSHEA was hailed as a victory for consumer access to dietary supplements and a defeat of government overregulation, the DSHEA has been widely criticized by medical, legal, and public groups as being deficient in safety provisions and requirements for scientifically proven claims. Citing reports of serious toxicity caused by substances regulated as dietary supplements, critics point out that Congress passed the Food, Drug, and Cosmetic Act of 1938 as a consequence of poisoning by sulfanilamide elixir and the Kefauver–Harris Amendments in 1962 in reaction to the thalidomide tragedy in Europe. Barring public outcry for congres-

sional action over a disastrous toxic effect, the slow process of FDA rule-making and litigation between the FDA and the dietary supplement industry will define the broad-based language of the DSHEA. By counseling consumers about possible lax manufacturing standards and potential drug interactions and adverse effects of dietary supplements, pharmacists can circumvent some of the inadequate safeguards of the DSHEA.[2,4,8,10,14–17]

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Directions for Clinical Practice in Pharmacy (Hilton Head Conference)

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INTRODUCTION

The ASHP Research and Education Foundation and the American Society of Hospital Pharmacists (ASHP) conducted an invitational consensus conference entitled "Directions for Clinical Practice in Pharmacy" on February 10–13, 1985. The conference was held in Hilton Head Island, South Carolina, and has come to be known as the Hilton Head Conference.[1] The conference included approximately 150 pharmacy practitioners and educators; in addition, others from medicine, nursing, and hospital administration were invited as observers.

SYNOPSIS

The goals for the development of consensus statements were to determine the status of the clinical pharmacy movement and to help the pharmacy profession to continue advancing clinical practice. The principal objectives of the conference were: 1) to examine to what extent the profession had established goals with respect to clinical practice, 2) to assess the current status of the clinical practice of pharmacy and pharmacy education, and 3) to identify practical ways by which clinical pharmacy could be advanced.

The keynote address, presented by Paul F. Parker, Sc.D., a consultant and retired director of pharmacy at the University of Kentucky, was entitled "Clinical Pharmacy's First 20 Years." Parker described clinical pharmacy as the most important practice, education, and professional philosophy in the history of pharmacy. He noted that clinical pharmacy will advance only by meeting the goals of quality care.

Accomplishing the conference goals required an exploration of four key topics: 1) pharmacy as a clinical profession, 2) barriers to clinical practice, 3) the symbiosis of clinical practice and education, and 4) building pharmacy's image. Plenary presentations were given on each topic, and these were followed by workshop discussions.

Charles D. Hepler, Ph.D., presented "Pharmacy as a Clinical Profession." His assessment of clinical pharmacy focused on the role of clinical pharmacy, how professional services are provided, the need to obtain professional authority, and the patient-oriented focus of clinical pharmacy. The workshops were charged with two tasks: 1) to determine whether there is a need for the term clinical pharmacy and, if so, to conceptually distinguish it from pharmacy and 2) to consider what steps are needed to establish pharmacy as a clinical profession. A total of 18 consensus statements resulted. The statements with the highest consensus among participants emphasized that the profession of pharmacy has a fundamental purpose to serve society for safe, appropriate, and rational use of drugs; to provide leadership to other healthcare professionals and the public to ensure responsible drug use; to provide authoritative, usable drug information; and to work collaboratively with other healthcare professions on health promotion and disease prevention through the optimal use of drugs. According to another statement, pharmacists are the professionals ultimately responsible for drug distribution and control, and the use of technicians, automation, and technology should be maximized to free time for pharmacists to perform clinical services. Ultimately, the purposes and goals of clinical pharmacy are the same as those of pharmacy, but clinical pharmacy stresses patient-oriented services and the association with patient outcomes.

To address the barriers to clinical practice, a panel discussed the "Realities of Contemporary Practice." The panelists were Chip Day, Robert P. Fudge, Teresa Volpone McMahon, Pharm.D., and Steven L. Smith, Pharm.D., and the session moderator was Dennis K. Helling, Pharm.D. Each panelist described routine activities in his or her practice and identified several barriers to clinical pharmacy, notably a lack of time. Ultimately, the panelists

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agreed that practicing clinical pharmacy had become easier within the past few years, mostly because of increased recognition by other healthcare professionals of the pharmacist's role in patient care. The workshop groups produced 37 consensus statements on barriers to clinical practice. According to the statements receiving the highest consensus, pharmacy directors are unable to provide effective leadership to their staff, a widely agreed-upon philosophy of pharmacy practice is lacking, there is no concurrence on what the standard of practice in pharmacy should be, consumer demand for clinical pharmacy services is weak because the public has a poor understanding of the services pharmacists can offer, and the value of clinical pharmacy services has not been adequately demonstrated.

To discuss the symbiosis of clinical practice and education, Charles A. Walton, Ph.D., presented the educator's perspective and Marianne F. Ivey presented the practitioner's perspective. The presenters believed that both pharmacy practitioners and educators should share in advancing the profession through the establishment and provision of clinical pharmacy services, through education and training of pharmacy students and pharmacists, and through clinical research. The objectives for the workshop groups were: 1) to identify steps for making more effective use of clinical pharmacy faculty in improving the level and quality of clinical pharmacy services and 2) to use pharmacy staff more effectively in clinical education. A total of 33 consensus statements were developed for objective 1 and 18 for objective 2. With respect to using clinical pharmacy faculty, it was agreed that there is a need to clearly define a shared philosophy between clinical faculty members and pharmaceutical services staff, the clinical service responsibilities of clinical faculty, and the clinical education missions of both the college and the pharmacy department. In addition, orienting deans and other academics to the roles of clinical faculty would provide a basis for balancing teaching, research, and service responsibilities and would help acknowledge the scholarly activity and clinical research that occur in clinical practice.

With respect to using pharmacy staff more effectively in clinical education, the major statements identified that staff should be recognized for their teaching activities; that staff involved in clinical instruction should participate in the evaluation of students; that hospital administrators, pharmacy directors, and staff should recognize their respective roles in pharmacy education and have a thorough understanding of the clinical faculty's responsibilities; and that educational programs should be developed to train pharmacists to manage clinical services.

William A. Miller, Pharm.D., presented the final plenary session on building pharmacy's image. According to Miller, building pharmacy's image as a clinical profession would occur simply by providing clinical services. Pharmacy would be advanced as a clinical profession by establishing goals for pharmaceutical services; creating standards for pharmacy practice; planning, implementing, and managing pharmaceutical service, education, and research programs; providing financial management; and assessing the quality of pharmaceutical services and drug use within the institution. The workshop groups sought to characterize the type of relationship pharmacy should establish with medicine, nursing, hospital administration, and the public. Eight consensus statements were written. The major consensus statement was that pharmacy should establish a public image of advocacy in all matters related to the use of drugs. Other statements expressed that pharmacist input should be a required component of the drug-use process, that pharmacy should be viewed as a clinical service, and that pharmacy is a colleague with nursing and medicine in patient care.

DISCUSSION

The Hilton Head Conference affirmed that pharmacy is a clinical profession committed to clinical practice and the patient. Pharmacy is fundamentally a healthcare profession with a responsibility for safe and effective drug use in society.

The conference provided a forum for pharmacists to discuss the past, present, and future of clinical pharmacy. Even though the conference occurred in 1985, many of the conclusions reached still apply to practice today. For instance, some of the barriers identified with respect to leadership and substantiation of the value of clinical pharmacy services still exist. Also, there continues to be a need to educate the public and gain the support of other healthcare professionals for clinical pharmacy practice.

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Disease Management

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INTRODUCTION

Pharmacy practice has evolved from a focus on the responsible dispensing of medications to a patient-oriented profession concerned with the optimum use of pharmaceutical products in the management of disease states. This new practice model, which is known as *pharmaceutical care*, emphasizes the role of pharmacists in meeting the health needs of patients through medication-related care.[1] Pharmaceutical care necessitates an ongoing collaboration with physicians and is often referred to as *collaborative drug therapy management*.[2] Pharmaceutical care is a form of *disease management*, a phrase which broadly encompasses coordinated healthcare by providers from complementary professions whose shared goal is the improvement of patient well-being.[3] Federal law requires that pharmacists offer medication counseling to patients receiving Medicaid benefits in the belief that such education will lead to more effective drug therapy.[4] In most states, this requirement is interpreted as a mandate compelling pharmacists to counsel all patients. Disease management extends the traditional duties of pharmacists from dispensing medications and counseling patients to include a more significant role in securing the success of drug therapy.

Managed care often forces health plan administrators to limit costs by limiting enrollee access to physicians, which creates a need for nonphysician involvement in patient care.[5] Chronic diseases are often accompanied by complex drug regimens that may lead to patient confusion and poor outcomes that further increase healthcare costs.[6] The knowledge and training of pharmacists in drug and disease interactions uniquely qualify them to assist in medication management. The distribution of pharmacists in the community enhances patient contact, and ideally situates pharmacists to assess therapeutic responses to prescribed therapies. Through education and accessibility, pharmacists can improve medication compliance and diminish the risk of adverse drug effects; and by monitoring and modifying drug therapy, pharmacists can assure that patients increase their chances for achieving favorable outcomes.[7] The potential to decrease healthcare costs provides a pharmacoeconomic incentive for involving pharmacists in disease management.[8]

SCOPE OF PRACTICE

Pharmacy involvement in disease management may entail educating patients on the desirable and undesirable effects of pharmaceutical products and on proper drug administration, therapeutic drug monitoring through laboratory testing and interpretation, or initiating and modifying medication regimens based upon ongoing assessments of physiologic response.[9] The disease states amenable to pharmaceutical care include asthma, diabetes mellitus, cardiovascular risk reduction, chronic pain management, mental health disorders, epilepsy, women's health concerns, infectious diseases, and anticoagulation therapy.[10] However, pharmacy involvement in any field of clinical care is only limited by the needs of patients and providers and the willingness and competence of pharmacists to participate. Although practiced in acute care hospitals, critical analyses of the potential benefits of pharmaceutical care have focused on drug therapy management of chronic diseases by community pharmacists in ambulatory settings. Pharmacy participation in the direct care of patients can be demonstrated in a concise review of several current programs.

The University of Mississippi School of Pharmacy has been an innovator in disease management for over a decade. One of its more successful Pharmaceutical Care Clinics addresses the community need to improve asthma management so that the overutilization of emergency care is curtailed. The backbone of the clinic is a protocol dictating diagnostic and therapeutic algorithms that were

adapted to local conditions from established national practice guidelines.[11] The care is fleshed out by educating patients as to the pathogenesis of asthma, the signs and symptoms of airway decompensation, and the pharmacology underlying medication options. Both short-term goals, lifestyle modifications such as smoking cessation and allergen avoidance, and long-term goals, such as decreased rates of school or work absenteeism, are set and reviewed. In concord with the physician-supervised protocol, an individualized asthma action plan is developed for each referred patient. Pharmacists train patients to use peak flow meters and to monitor and self-adjust drug therapy. Pharmaceutical care is intended to supplement regularly scheduled physician appointments, to identify and respond to intervening pathophysiology, and to mitigate the need for urgent medical attention.

Outcome analysis reveals that the Asthma Care Clinic at the University of Mississippi is achieving its stated goals.[12] Utilizing enrolled patients as historical controls, this disease-management intervention resulted in fewer emergency room visits or hospitalizations for asthma decompensation. An annualized cost saving of approximately 60 percent for these hospital services has been realized. Cost savings are sustained even though additional clinical funds are expended on pharmaceutical care. As a result of these salutary findings, all patients presenting for the emergency treatment of asthma-related bronchospasm at the University Medical Center are subsequently considered for disease-management assessment.

Similarly encouraging results of collaborative drug therapy are reported in the medical literature for a number of economically burdensome chronic diseases. Project ImPACT (Improve Persistence and Compliance with Therapy): Hyperlipidemia assessed the contributions of community pharmacists to the care of patients with lipid disorders requiring pharmacologic intervention.[13] During this three-year project, the observed rate for compliance with lipid-lowering medication therapy improved to approximately 90 percent. The impact of these Virginia pharmacists was significant, as nearly two-thirds of participants achieved and maintained nationally recognized treatment goals. The City of Asheville, North Carolina, and the largest private employer in western North Carolina, the Mission St. Joseph Health System, contracted with trained community pharmacists to manage the drug therapy of their employees with diabetes.[14] Patient interaction with providers increased with the advent of pharmaceutical care, while metabolic indices of disease control improved. Moreover, payer expenditures for the total cost of ambulatory and inpatient diabetes care decreased. When absentee rates were compared to prior years, participants worked an average of 6.5 days more per year during the project. Pharmacy disease management favorably impacted both direct and indirect medical costs. The majority of employees were highly satisfied with their care, as they reported improvements in functional status and quality of life.

A critical review of pharmacy disease management programs is hindered by the lack of statistical design rigor and robust cost analyses found in many published reports. The heterogeneity of studies with regard to clearly defined and widely accepted outcome measures also hampers systematic assessment. The authors of a review of 55 comparative studies representing 50 programs in which pharmacists provided support for ambulatory care providers in outpatient clinics and community pharmacies found that prescription monitoring led to a general trend toward cost savings, enhanced timeliness of care, and improved clinical outcomes.[15] However, this review noted no consistent improvement in disease knowledge or patient satisfaction and little improvement in quality of life among pharmaceutical care enrollees. The National Institutes of Health (NIH) through the Agency for Healthcare Research and Quality (AHRQ) is funding studies to address these deficiencies in the evidence base.[16] This federal interest in data documenting the costs and benefits associated with disease management bodes well for the acceptance of pharmaceutical care into the medical mainstream.

CREDENTIALING AND CERTIFICATION

As pharmacy embraces disease management, the profession must reassure skeptics that pharmacists possess the necessary knowledge and skills to provide these services. For pharmacists desiring to broaden their scope of practice, training beyond that required to obtain a pharmacy degree or license may be necessary. Although credentialing is a controversial topic, it is increasingly evident that a nationally recognized process is necessary to bolster the professional stature of pharmacists and to identify clinical specialists who are capable of providing reimbursable pharmaceutical care.

Credentialing is defined in a medical context as the process by which an organization or institution obtains, verifies, and assesses an applicant's qualifications to provide a particular patient-care service. The Council on Credentialing in Pharmacy (CCP), a coalition of 11 national organizations founded in 1999 as a coordinating body for credentialing programs, delineates three avenues for credentialing in pharmacy: 1) credentials required to enter the profession—academic degrees, 2) credentials required to enter practice—licenses, and 3) optional cre-

dentials documenting specialized knowledge and skills—advanced academic degrees or certificates.[17] Certification involves granting a credential to a pharmacist who has demonstrated a level of competence in a specific and relatively narrow area of practice. Postlicensure certification usually requires an initial assessment and periodic reassessments of a grantee's qualifications. There are three agencies that offer certification to pharmacists: the Board of Pharmaceutical Specialties (BPS), the Commission for Certification in Geriatric Pharmacy (CCGP), and the National Institute for Standards in Pharmacist Credentialing (NISPC). BPS was established by the American Pharmaceutical Association (APhA) in 1976 and certifies pharmacists in five practice concentrations: nuclear pharmacy, nutrition support pharmacy, oncology pharmacy, psychiatric pharmacy, and pharmacotherapy. An "Added Qualifications" in either infectious diseases or cardiovascular pharmacy is available for pharmacists certified in pharmacotherapy. The CCGP was established by the American Society of Consultant Pharmacists (ASCP) in 1997 and supervises the certification program in geriatric pharmacy practice. NISPC was founded in 1998 to oversee pharmacist credentialing in disease management.

NISPC is composed of four member organizations: the APhA, the National Association of Boards of Pharmacy (NABP), the National Association of Chain Drug Stores (NACDS), and the National Community Pharmacy Association (NCPA).[18] NISPC was charged with coordinating the development of a nationally recognized testing program to credential pharmacists in disease-specific pharmaceutical care. NISPC utilized NCPA's National Institute for Pharmacist Care Outcomes (NIPCO) model as a resource for constructing examinations to test disease-management competencies. An expert panel drawn from community practitioners, academicians, pharmacy benefits managers, and state board of pharmacy members develops the standards and objectives for each disease-management examination. Panel members ensure that the content of the examinations reflects the knowledge base expected of pharmacists providing care at an advanced practice level.

The first pharmacy disease-management examinations were offered in 1998 as pencil-and-paper tests in the states of Arkansas, North Dakota, and Mississippi.[19] Certification was offered in four disease states: asthma, dyslipidemia, diabetes, and anticoagulation therapy. Since that time, the examinations have been adapted for computer administration at multiple test sites any time of the year. However, non-electronic testing is offered annually at the APhA national meeting. Due to the specialized funds of knowledge required for successful certification, pharmacists are strongly encouraged to have at least 2 years of experience in the field being tested prior to applying for examination. States may require that prerequisites, such as a training program, be completed before permission for testing is granted. The NISPC-sanctioned examinations are graded as either pass or fail; a score of 75% or greater yields a passing grade. Pharmacists receiving a passing score are eligible for this recognition to be listed on the NABP's Pharmacist and Pharmacy Achievement and Discipline (PPAD) Web site database (Table 1).

Since 1998, NISPC has awarded credentials to over 1,200 pharmacists in the United States. In 2001, NISPC adopted the designation of Certified Disease Manager (CDM) for those pharmacists successfully completing one of the disease-management exams. NISPC hopes the CDM credential will gain national recognition by both patients and payers. NISPC certification must be renewed every 3 years. For pharmacists awarded a CDM credential in 2000 or later, 30 hours of American Council on Pharmaceutical Education (ACPE)–approved continuing education in the credentialed disease state must be documented within the 3-year recertification period. Ten of the required 30 hours must be obtained during the third year.

The availability of a cadre of pharmacists certified in disease management does not assure reimbursement for pharmaceutical care. NISPC formed a Standards Board and a Payer Advisory Panel to ensure public trust in the care provided through collaborative drug therapy by credentialed pharmacists. The Standards Board has identified a need to improve the communication skills of pharmacists so that their collaborative work is enhanced, to train pharmacists regarding the benefits of nonpharmacologic therapies, and to adopt a regular review and modification process for disease-management competencies. The Payer Advisory Panel was tasked with advising NISPC on the needs of the payer community as pharmaceutical care penetrates the marketplace. The Panel has stressed the need to clearly define the package of clinical services credentialed pharmacists provide, to involve other allied health professionals in collaborative management, to develop standard outcome measures, and to establish an accessible databank for credentialed pharmacists. The work of the Standards Board and Payer Advisory Panel should significantly contribute to the stature of pharmaceutical care.

REIMBURSEMENT

In 1998, Mississippi became the first state to secure government reimbursement for pharmaceutical care.[20]

Table 1 Disease management resources

Professional Organizations		E-mail	Phone
Academy of Managed Care Pharmacy	AMCP	www.amcp.org	800-827-2627
American Association of Colleges of Pharmacy	AACP	www.aacp.org	703-739-2330
American College of Apothecaries	ACA	www.acaresourcecenter.org	901-383-8119
American College of Clinical Pharmacy	ACCP	www.accp.com	816-531-2177
American Council on Pharmaceutical Education	ACPE	www.acpe-accredit.org	312-664-3575
American Pharmaceutical Association	APhA	www.aphanet.org	202-628-4410
American Society of Consultant Pharmacists	ASCP	www.ascp.com	703-739-1300
			800-355-2727
American Society of Health-System Pharmacists	ASHP	www.ashp.org	301-657-3000
National Association of Boards of Pharmacy	NABP	www.nabp.net	847-698-6227
National Association of Chain Drug Stores	NACDS	www.nacds.org	703-549-3001
National Community Pharmacists Association	NCPA	www.ncpanet.org	703-683-8200
			800-544-7447
Certifying Bodies			
Anticoagulation Forum	ACF	www.acforum.org	617-638-7265
Board of Pharmaceutical Specialties	BPS	www.bpsweb.org	202-429-7591
Commission for Certification in Geriatric Pharmacy	CCGP	www.ccgp.org	703-535-3038
Association of Asthma Educators	AAE	www.asthmaeducators.org	888-988-7747
National Certification Board for Diabetes Educators	NCBDE	www.ncbde.org	847-228-9795
National Institute for Standards in Pharmacist Credentialing	NISPC	www.nispcnet.org	703-299-8790
Industry Liaisons			
Disease Management Association of America	DMAA	www.dmaa.org	202-861-1490
Disease Management Purchasing Consortium and Advisory Council	DMC[2]	www.dismgmt.com	781-237-7208

(Adapted from Ref. [17].)

The Health Care Financing Administration (HCFA) approved payment through the Mississippi Division of Medicaid to pharmacists for disease-management services provided to patients enrolled in the Medicaid program. The components of a reimbursable service are patient evaluation, patient or caregiver education, drug therapy review and compliance assessment, and disease management under protocol according to clinical practice guidelines. NISPC credentialing is currently required for pharmacists to apply for a Mississippi Medicaid provider number, which in turn is necessary to bill for pharmaceutical care under the Other Licensed Practitioner designation.

In addition to obtaining a Medicaid provider number, a pharmacist must produce two other documents prior to providing pharmaceutical care in Mississippi: a written evaluation and treatment protocol and a referral from a physician. The protocol must define the collaborative agreement between the pharmacist and the referring physician and be on file with the State Board of Pharmacy. The nature of protocol requirements differs among practice sites. Within an institution, one protocol agreement may be submitted for all the physicians practicing at that site for use by all their referred patients. In the community setting, a separate protocol from each referring physician must be completed for each patient. Pharmacists are paid a flat fee for each 15- to 30-minute patient encounter. Currently, pharmacists can be reimbursed for up to 12 visits per year per patient for all disease states managed. These pharmaceutical care visits are in addition to the annual allotment of reimbursed physician visits provided by Mississippi Medicaid. No restrictions exist as to the number of patients a pharmacist can manage.

Mississippi is not alone in explicitly recognizing the important contributions of pharmacists to disease management with state funding. In 2000, the Iowa Division of Medicaid initiated a reimbursement program for pharmaceutical case management.[21] During this 2-year pilot project, patients who are candidates for pharmaceutical care are identified and participating pharmacists are notified of their eligibility. The pharmacist performs an initial disease assessment and develops an individualized therapeutic plan for each patient, which is subsequently reviewed by a physician collaborator. Pharmacists must meet criteria outlined by the project's advisory commit-

tee, and complete a training program approved by the Iowa Department of Human Services. New Mexico also has a demonstration project that allows for pharmaceutical care under physician-supervised protocol.[22] Assessments of the medical and cost outcomes of these projects will determine the future of these initiatives.

State support for pharmaceutical care is bolstered by managed care imperatives. States are increasingly willing to fund programs that maintain the health of their insured populations, if this care can be proven to be efficacious and to control medical costs. States are confronting the same financial challenges faced by private health plan leaders such as Humana and Kaiser Permanente, who were early adopters of disease management. Health Maintenance Organizations (HMOs) employ pharmaceutical care to improve the health of their enrollees and thus limit the need for costly medical interventions.[23] HMOs have invested considerable time and effort into developing multidisciplinary treatment pathways and algorithms for many pharmacy-intensive disorders and diseases.[24] By standardizing processes of care, providers become accountable for fully implementing therapies proven to favorably impact patient outcomes. The dedication of organized pharmacy to disease management is likely to lead states to commit greater resources to pharmaceutical care.

As Medicare becomes structured to support health maintenance, federal interest in disease management is coming full circle. The Indian Health Service was a pioneer in pharmaceutical care, and the U.S. Armed Forces and Veterans Affairs healthcare sectors are now leaders in collaborative drug therapy.[25] In 1999, HCFA recognized the provider status of nonfederally employed pharmacists to participate in diabetes management.[26] Congress and the Medicare Trust administrators are actively weighing the benefits of extending coverage to include disease management by pharmacists. Pharmacists are likely to be accorded enhanced provider status given the developing affirmative body of research and patient willingness to embrace pharmaceutical care. Indeed, a recent patient survey indicated that a majority would pay for disease management by pharmacists, if accredited services were widely available.[27]

Although reimbursement is often cited by pharmacists as the paramount barrier to the widespread dissemination of disease management, other troublesome yet surmountable obstacles exist.[28] Even when reimbursement is assured, the requirements accompanying billing can be time-consuming and costly. As in other medical fields, the paperwork required to document encounters and apply for pharmacy service reimbursement from various payers in different practice settings is not uniform. The information systems in place in most community pharmacies are often inadequate to respond to the additional demands of disease management.[29] These administrative concerns compound the stresses placed on pharmacists by the high volume of medication dispensing and the need for technician supervision characteristic of retail pharmacy practice. These issues will need urgent attention so that the willingness of the public and payers to support pharmaceutical care is not hindered.

REGULATORY AND ETHICAL ISSUES

Laws pertaining to disease management differ from state to state. Most states provide the Board of Pharmacy with statutory authority to regulate pharmaceutical care. Thirty-three states currently allow pharmacists to initiate or modify drug therapy pursuant to a collaborative practice agreement or protocol; other states are in the process of amending their practice acts to incorporate pharmaceutical care services (Table 2). Pharmacists must adhere to the restrictions imposed by state practice agreements or they assume a greater risk of liability. Exposure to administrative or criminal penalties can be diminished if pharmacists fully acquaint themselves with the boundaries limiting pharmaceutical care in their state.

One legislative initiative is worthy of note. North Carolina allows a pharmacist who provides disease management to be designated as a Clinical Pharmacy Practitioner.[30] Pathways to attain this professional recognition are available to either bachelor or doctorate degree–holding pharmacists. Applicants for this designation must submit a collaborative practice agreement that delineates the dimensions of their pharmaceutical care proposal for formal review. Approval is granted after appraisal by both the Board of Pharmacy and State Medical Board. Many in organized medicine have joined pharmacy in endorsing a grant of proscribed prescriptive authority to pharmacists through such novel state provisions. However, the American Medical Association (AMA) opposes nonphysician groups that seek independent prescribing rights as they believe this will further fragment healthcare.[31] A more recent Position Paper outlining the stance of the American College of Physicians-American Society of Internal Medicine (ACP-ASIM) with regard to the increasing scope of pharmacy practice endorses further research on pharmaceutical care programs, yet opposes independent pharmacist prescriptive privileges and the initiation of drug therapy.[32]

Some within the pharmacy profession also question whether direct patient care is a proper role for pharmacists.[33] They argue that disease management requires

Table 2 Disease management by state

State	Practice pursuant to collaborative agreement or protocol	Practice setting	Comments
Alaska	Yes	All	Drug administration allowed
Arizona	Yes	Institutional settings, community health center	Drug administration allowed
Arkansas	Yes	All	Administer drugs by injection allowed
California	Yes	Licensed healthcare facilities, clinics, home care settings	Administer drugs by injection allowed
Florida	Yes	All	Prescriptive authority restricted to formulary drugs Protocol-based dependent prescribing pending
Georgia	Yes	All	Restricted to modifying drug regimen
Hawaii	Yes	Licensed acute care hospitals	Restricted to modifying drug regimen Administer drugs by injection allowed
Idaho	Yes	All	Drug administration allowed
Indiana	Yes	Acute care settings, private mental health institutions	Drug administration not prohibited
Kansas	Yes	All	By delegation of physician
Kentucky	Yes	All	Drug administration allowed
Louisiana	Yes	All	Drug administration allowed
Michigan	Yes	All	Drug administration allowed
Minnesota	Yes	All	Restricted to modifying drug regimen Administer drugs by injection allowed in first doses and in medical emergencies
Mississippi	Yes	All	Administer drugs by injection allowed
Montana	Yes	All	Drug administration allowed
Nebraska	Yes	All	Restricted to monitoring drug therapy Administer drugs by injection allowed
Nevada	Yes	Licensed medical facilities	Immunizations by protocol
New Mexico	Yes	All	Limited to Pharmacist Clinician, eligible to register with Drug Enforcement Administration
North Carolina	Yes	All	Recognizes Clinical Pharmacy Practitioner
North Dakota	Yes	Institutional settings, clinics	Drug administration allowed
Ohio	Yes	All	Restricted to modifying drug regimen Drug administration allowed
Oregon	Yes	All	Restricted to modifying drug regimen Drug administration allowed
Rhode Island	Yes	Hospital (including outpatient clinics), nursing homes	
South Carolina	Yes	All	Drug administration allowed
South Dakota	Yes	All	Administer drugs by injection allowed
Texas	Yes	All	Administer drugs by injection allowed
Utah	Yes	All	Physician Licensing Board approval necessary for outpatient services
Vermont	Yes	Institutional settings	Restricted to modifying drug regimen Drug administration allowed
Virginia	Yes	All	Restricted to modifying drug regimen Drug administration allowed
Washington	Yes	All	Administer drugs by injection allowed
Wisconsin	Yes	All	Guideline Drug administration allowed under protocol with prescriber
Wyoming	Yes	All	Administer drugs by injection allowed

(Adapted from Refs.[2],[42–45].)

proficiency in differential diagnosis, analytical thinking, and patient interaction skills that are not within the purview of pharmacists. They believe that pharmacy should retain its traditional focus on quality assurance in medication delivery and cede responsibility for patient care to physicians rather than join the ranks of other mid-level practitioners. These concerns are being addressed in undergraduate and postgraduate pharmacy education. Pharmacy schools are moving away from passive teaching models to active curricula founded on problem-based learning and from didactic lectures to clinical pharmacy preceptorships in practice environments. Pharmacy leaders are also addressing the lack of readily available advanced clinical training for community pharmacists.

Pharmaceutical care is not without its extramural critics as well. Consumer advocates question whether disease management is a sound public health policy.[34] According to these critics, such programs concentrate healthcare expenditures on high-risk patients to control short-term costs and thus redirect scarce resources needed for health promotion and disease prevention. They believe that disease management has been promoted by the pharmaceutical industry as a way to augment drug sales. Drug manufacturers are accused of organizing disease-management programs to gain access to restricted formularies and to ensure control over medication demands rather than to improve patient care.[35] The research community also raises ethical concerns, as it objects to the lack of public reporting of the outcomes from commercial pharmaceutical care programs.[36] It cautions that while exclusive access to proprietary information may be necessary to preserve a company's competitive advantage, it may hinder medical progress. Pharmacists must be wary of uncritically adopting pharmaceutical care protocols developed by the for-profit sector and be vigilant to unethical inducements to prescribe unnecessary or inappropriate medication therapies.

Public regard for the honesty and ethical character of pharmacists is greater than for either physicians or the clergy.[37] Pharmacy must guard against a decline in consumer confidence as it expands its spectrum of services. Professional codes are being challenged by the new relationships developing between pharmacists and those they serve. As pharmacists become more involved in direct patient care, their ethical obligations extend beyond professional dictates to maintain knowledge and skills to uphold the welfare of patients. Of significant patient concern are the related issues of privacy and confidentiality. Therapeutic relationships are built on a foundation of trust. Clinicians are entrusted with sensitive, personal information by patients and they are expected to hold these private communications in strict confidence by the canons of medical ethics.[38] Additionally, respect for the dignity of patients entails promoting their autonomy: the right of patients to inform and to govern their own healthcare decisions. However, pharmacists practicing in collaborative arrangements have ethical duties to each party to the agreement, to both patients and physicians. Conflicts can arise as patients may provide information to a pharmacist that they are unwilling to share with their physician.[39] A pharmacist may be faced with the moral dilemma of disclosing information provided in confidence or withholding data pertinent to medical decision making. In a purely consultant relationship, the primary duty of the consultant is owed to the party requesting the consultation and professional standards hold that full disclosure is warranted. Disease management is an effort by both pharmacists and physicians on the behalf of patients and thus the desires of patients for confidential interactions may be ethically problematic. The importance of these ethical principles is reflected in recent federal legislation; the Health Insurance Portability and Accountability Act requires the establishment of health privacy regulations to protect the confidential information yielded by patients.[40] Pharmaceutical care is more covenant than contract; when the inevitable conflicts arise, pharmacists must recognize that resolution may require choices based upon individual patient values rather than on a reflexive recourse to an objective standard. As disease management takes hold, comprehensive pharmacy education will need to encompass legal and ethical training so that pharmacists retain the good will of the public they currently enjoy.

SUMMARY AND CONCLUSION

National surveys estimate that one-third of adults in the United States suffers from a chronic disease, yet most fail to achieve treatment goals promulgated by consensus care guidelines; fewer than one half of hypertensives have well-controlled blood pressure and less than one-quarter of patients with coronary artery disease have lipid levels within optimal limits.[41] The current healthcare model is geared to acute disorders, rather than tooled for the systematic care of chronic diseases. Pharmacy disease management is the multidisciplinary process of selecting appropriate drug therapy and continually monitoring patient outcomes to that therapy. It is a response to the demands of health-conscious consumers and cost-conscious payers. The value of pharmaceutical care can be promoted by ensuring the knowledge and judgment of practitioners through training and credentialing and by measuring their impact on health outcomes through rigorously designed clinical trials. Healthcare is in transition, and new models of delivery will likely be accompanied by a broader pharmacoeconomic perspective, one that does not isolate drug costs, but views the cost of

pharmaceutical care in the overall context of medical care. Pharmacy is favorably situated to contribute to disease management and to profit from this fundamental shift in the healthcare paradigm.

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PROFESSIONAL DEVELOPMENT

Doctor of Pharmacy

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INTRODUCTION

The doctor of pharmacy (Pharm.D.) degree is the professional degree awarded to graduates of a U.S. school or college of pharmacy who have completed a minimum of 6 years of academic course work. The degree is required to take a board examination to become licensed as a pharmacist.

HISTORY OF THE Pharm.D. DEGREE

The awarding of the Pharm.D. degree in the United States dates back to the turn of the twentieth century. Prior to the 1900s, there were no standardized education requirements to become a pharmacist in the United States. One needed only the requisite knowledge to pass a board exam, and this knowledge could be obtained through apprentice programs, correspondence courses, "cram schools," home study programs, or other means. Each course of study offered its own credentials for successful completion. In 1892, the University of Wisconsin introduced the first bachelor's course in pharmacy, and in 1904, New York became the first state to require a school diploma to practice pharmacy.[1] By 1900, there were about 55 pharmacy schools in the United States, but less than 10% of pharmacists had attended a school or college of pharmacy. Common pharmacy "degrees" awarded in the United States at this time included the Ph.G. (Graduate in Pharmacy); Ph.C. (Pharmaceutical Chemist); Ph.D., Phm.D., Pharm.D., or P.D. (Doctor of Pharmacy); Pharm.M. or Ph.M. (Master of Pharmacy); and B.S. (Bachelor or Science in Pharmacy).[2]

In the 1920s, pharmacy education became more standardized. In 1927, the American Association of Colleges of Pharmacy (AACP) adopted "Basic Material for a Pharmaceutical Curriculum," and in 1928, its member schools approved a resolution requiring at least 4 full college years of at least 30 weeks each for graduation from a pharmacy program.[2] In 1932, the American Council on Pharmaceutical Education (ACPE) was formed, and pharmacy schools now had a formal mechanism by which to be evaluated for purposes of accreditation.

During the 1920s and 1930s, the Pharm.D. degree underwent several transformations. In 1925, institutions were allowed to offer the Pharm.D. degree after candidates completed not less than 3 years of graduate work. In 1932, the degree was officially defined and required not less than 3 years of graduate work for a total of 7 years of undergraduate and graduate work. In 1934, members schools of AACP restricted schools from offering pharmacy degrees other than a B.S. or B.S. Pharmacy. It was decided at that time that the Pharm.D. degree could not be awarded after 1938.[1,2]

In the 1940s, there was talk among pharmacy educators to increase the length of the baccalaureate degree from 4 to 5 years and perhaps to resurrect the Pharm.D. degree. World War II had begun, and just as in World War I, pharmacy was not viewed by the U.S. armed forces as an academic profession. Pharmacy students were refused deferments, and pharmacy graduates were refused commissioned officer status.[2,3] Concurrently, sulfa drugs and other antibiotics, as well as hormones, had been developed into dosage forms, and there was an emerging knowledge explosion in the pharmaceutical sciences. These events prompted educators to define a 6-year doctoral program comprised of an expanded prepharmacy curriculum of general courses and a highly science-based pharmacy curriculum. This, in turn, led to "The Pharmacy Survey of 1946–48," in which the ACPE surveyed pharmacy faculty and practitioners to determine future directions for pharmacy education.[2]

As the 1940s came to a close, both AACP and ACPE granted approval to reinstate the Pharm.D. degree for a 6-year course of study, and in 1950, the University of Southern California became the first pharmacy school to adopt the 6-year Pharm.D. as its only professional degree leading to licensure as a pharmacist. Discussion among pharmacy educators continued regarding the length of the baccalaureate degree. In the early 1960s, AACP recom-

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mended that the baccalaureate curriculum in pharmacy be extended to 5 years, and in 1965, the 5 year degree became the minimum standard.[2] Pharmacy schools were now able to offer a baccalaureate or a Pharm.D. degree as their entry-level degree into the profession. They could also offer the PharmD as a postbaccalaureate degree, a 1- to 3-year program after completion of the B.S. degree. A third option was the "track in" PharmD, whereby all students began as baccalaureate students, and a few students were allowed to enter the Pharm.D. curriculum after completing a certain number of their baccalaureate courses. For the next 25 years, debates raged over the length of study and titles of pharmacy degrees.

The 1960s through the 1980s witnessed the slow transformation of pharmacists' roles from solely dispensing to more patient and information centered. During the early 1960s, a few pharmacists—including Donald Brodie of the University of California–San Francisco, Donald Francke of the University of Michigan, and Paul Parker of the University of Kentucky—envisioned new roles for pharmacists. They saw the pharmacist working side by side with physicians to provide information about the potent new drugs that were being manufactured. Thus began the clinical pharmacy movement. By 1967, the first journal devoted to clinical pharmacy, *Drug Intelligence and Clinical Pharmacy*, was published. In 1972, two therapeutics textbooks that were centered around clinical pharmacy were published. By the mid-1970s, the U.S. government began to recognize the clinical contributions of pharmacists and passed legislation that required monthly reviews of drug regimens for patients residing in skilled nursing facilities.[3]

By the early 1970s, debates over pharmacy manpower, pharmacists' roles, and pharmacy education were heightened. In 1972, AACP President Arthur Schwarting recommended the formation of a "Commission on Pharmacy" to study the scope of pharmacy services in health care and to project the educational requirements needed to train pharmacists to provide these services. The commission was chaired by John S. Millis, President of the National Fund for Medical Education. The Millis Commission's report, "Pharmacists for the Future," was published in 1975.[2,3] The report contained 14 recommendations for pharmacy practice and education. Among these were continued movement of pharmacy as a knowledge-based clinical profession, increased development of clinical practice sites for pharmacy school faculty, and development of a national board licensing exam for pharmacists.

As a result of the Millis Commission's report, many pharmacy educators believed the time was right to adopt the Pharm.D. degree as the sole degree leading to licensure. In July 1978, the AACP's House of Delegates voted on the entry-level degree issue. By an almost two-to-one majority, the delegates voted to retain both the baccalaureate and Pharm.D. dual-degree structure.

In an article published in 1987 titled, "The Third Wave in Pharmaceutical Education: The Clinical Movement," pharmacy educator Dr. Charles D. Helper described his vision of pharmacy education and practice.[4] He described clinical pharmacy as adding new knowledge for the patient's welfare. This knowledge had limitations because it was provided to other health care providers for the patient's benefit, instead of being provided directly to the patient. Hepler wrote:

> As pharmacy further clarifies its clinical role, it should underscore its acceptance of as much responsibility for drug use control as its social authority (under law) will support. This ideal can be called pharmaceutical care: a covenantal relationship between a patient and a pharmacist in which the pharmacist performs drug use control functions (with appropriate knowledge and skill) governed by awareness of and commitment to the patient's interest. The term is intended to invoke analogies with the ideals of medical care and nursing care.

It was this concept of pharmaceutical care that rekindled the discussion of pharmacy curricula, degrees, and practice.

By 1989, over 50% of all U.S. pharmacy schools still offered only the baccalaureate degree as their entry-level degree, 14% offered only the Pharm.D. degree, and 30% offered both degrees.[2] AACP President William Miller appointed a task force (which was termed the Commission to Implement Change in Pharmaceutical Education) to develop recommendations to guide pharmaceutical education to meet the changing demands of the profession, the health care system, and society. During the next 2 years, the task force addressed the educational standards necessary for the entry-level curriculum for pharmacy students, the length of the curriculum, and the title of the degree granted for completing the curriculum. The commission's recommendations were published as a two-part series in 1991.[5,6] The recommendations included "an entry-level educational program for pharmacy practice that is at the doctoral level, is a least four professional, academic years in length, and follows pre-professional instruction of sufficient quality and length (two-year minimum) to prepare applicants for doctoral level education." Furthermore, the task force recommended the Pharm.D. degree as the sole degree for entry into pharmacy practice. In addition, schools and colleges that currently offered Pharm.D. programs were urged to examine, analyze, and revise their curricula to ensure

that they were based on and reflected the philosophy of pharmaceutical care.

In late 1989, the ACPE, in its regular periodic review of accreditation standards and guidelines, issued a "declaration of intent."[3] In this declaration, ACPE stated that its intent was to accredit only Pharm.D. degree programs as the entry-level degree into the profession and suggested the year 2000 as a probable target date. This declaration fueled much discourse among pharmacy educators, practitioners, and organizations. Educators were skeptical of obtaining adequate resources to add another year to their curricula. Practitioners were fearful that baccalaureate practitioners would be disenfranchised if pharmacy schools and colleges produced only doctoral-level graduates. Various pharmacy organizations were wary of the economic and political ramifications of such a decision.

During the next 3 years, a number of meetings were held and articles written regarding the future of pharmacy education, particularly with respect to the Pharm.D. degree. A joint statement by the American Pharmaceutical Association, the American Society of Hospital Pharmacists (now the American Society of Health-System Pharmacists), and NARD (now the National Community Pharmacists Association) supported a new Pharm.D. degree as the entry-level degree for practice in the profession of pharmacy and outlined methods of degree equivalence for current practitioners. In defining the new degree, the joint statement stressed, "It is the responsibility of pharmaceutical education to provide a graduate prepared for immediate licensure and commencement of a career in any area of pharmacy practice." Therefore, the joint statement urged that the degree requirements prepare pharmacists for entry into the practice rather than for specialty practice.[7]

Debates about the PharmD as the entry-level degree had continued for more than half a century, but the issue was finally resolved in July 1992, in Washington, D.C., at the annual meeting of the AACP. With every school and college of pharmacy casting one administrative and one faculty vote each, the delegates voted overwhelmingly to endorse the Pharm.D. degree as the sole degree leading into the practice of pharmacy. It was then up to the ACPE to finalize the accreditation standards and up to the individual colleges and schools of pharmacy to revise their respective curricula.

THE Pharm.D. CURRICULUM

As defined in the ACPE's standards for accreditation, the purpose of the Pharm.D. curriculum is to prepare students to become generalist practitioners of pharmacy.[8] Specifically stated in the accreditation standards,

> The goals and objectives of the curriculum in pharmacy should embrace the scope of contemporary practice responsibilities as well as emerging roles that ensure the rational use of drugs in the individualized care of patients as well as in patient populations. The organized program of study should provide students with a core of knowledge, skills, abilities, attitudes, and values that are necessary to the provision of pharmaceutical care and should provide opportunity for selection by students of courses and professional experiences in keeping with particular interests and goals. The need for life-long learning should be reflected as an integral theme of the curriculum.

The Pharm.D. degree requirements include postsecondary preprofessional courses and requirements, as well as a minimum of 4 academic years to achieve professional competencies. Most pharmacy schools and colleges require a minimum of 6 academic years to complete all the degree requirements. The preprofessional requirements include basic sciences (e.g., general chemistry, organic chemistry, biological sciences, mathematics, computer technology, physical sciences). In addition, the student should have adequate preparation in general education requirements such as humanities, behavioral sciences, social sciences, and communication skills.

The professional courses in the Pharm.D. curriculum consist of didactic material, laboratory courses, and practical experiences in patient care environments. The overall curriculum is structured to provide instruction in the following core areas: biomedical sciences (including anatomy, physiology, pathophysiology, microbiology, immunology, biochemistry, molecular biology, and biostatistics); pharmaceutical sciences (including medicinal chemistry, pharmacognosy, pharmacology, toxicology, and pharmaceutics); behavioral, social, and administrative pharmacy sciences (including health care economics, pharmacoeconomics, practice management, communications applicable to pharmacy, the history of pharmacy, ethical foundations to practice, and social and behavioral applications and laws pertaining to practice); pharmacy practice (including prescription processing, compounding and preparation of dosage forms, drug distribution, drug administration, epidemiology, pediatrics, geriatrics, gerontology, nutrition, health promotion and disease preention, physical assessment, emergency first care, clinical laboratory medicine, clinical pharmacokinetics, patient evaluation and ordering medications, pharmacotherapeutics, disease state man-

Table 1 American council on pharmaceutical education: standard for professional competencies and outcome expectations

Professional competencies that should be achieved through the College or School of Pharmacy's curriculum in pharmacy are an ability to

1. Evaluate drug orders or prescriptions accurately and safely, compound drugs in appropriate dosage forms, and package and dispense dosage forms.
2. Manage systems for storage, preparation, and dispensing of medicines, and supervise technical personnel who may be involved in such processes.
3. Manage and administer a pharmacy and pharmacy practice.
4. Apply computer skills and technological advancements to practice.
5. Communicate with health care professionals and patients regarding rational drug therapy, wellness, and health promotion.
6. Design, implement, monitor, evaluate, and modify or recommend modifications in drug therapy to ensure effective, safe, and economical patient care.
7. Identify, assess, and solve medication-related problems, and provide clinical judgment as to the continuing effectiveness of individualized therapeutic plans and intended therapeutic outcomes.
8. Evaluate patients and order medications and/or laboratory tests in accordance with established standards of practice.
9. Evaluate patient problems and triage patients to other healthcare professionals as appropriate.
10. Administer medications.
11. Monitor and counsel patients regarding the purposes, uses, and effects of their medications and related therapy.
12. Understand relevant diet, nutrition, and nondrug therapies.
13. Recommend, counsel, and monitor patient use of nonprescription drugs.
14. Provide emergency first care.
15. Retrieve, evaluate, and manage professional information and literature.
16. Use clinical data to optimize therapeutic drug regimens.
17. Collaborate with other healthcare professionals.
18. Evaluate and document interventions and pharmaceutical care outcomes.

(From Ref. [8].)

agement, outcomes documentation, self-care/nonprescription drugs, and drug information and literature evaluation); and professional experience (including introductory and advanced practice experiences acquired throughout the curriculum). Specific professional competencies common to all pharmacy curricula are listed in Table 1.

As depicted in Fig. 1, the pharmacy curriculum is grounded in the philosophy of providing pharmaceutical care to patients. The process begins by identifying therapeutics goals and outcomes for a patient's medical problem. Although this is usually done by physicians and other diagnosticians, pharmacists may provide information to assist with identifying these goals. In addition, pharmacists must make their own therapeutic decisions with regard to recommending nonprescription drug therapy. Once the role of medication has been determined, the correct drug, dosage form, dose, route of administration, and dosing schedule must be determined. Pharmacists must determine that these parameters are consistent with the patient's medication condition(s) and individual characteristics. The medication order is then filled and dispensed, with appropriate information regarding medication administration, storage, and side effects being given to the patient, their caregiver, or another healthcare professional. The effects of the drug must be monitored to determine whether the medication is working and whether it is producing any undesirable effects. Based on all this information, the patient's therapeutic goals may need to be readjusted.

A typical Pharm.D. curriculum contains didactic and laboratory courses as well as practice experiences. The didactic courses can be taught via traditional classroom lectures, through technology-based applications (e.g., computer applications, Web-based instruction, or other means of distance learning), or as independent study courses. They may represent discrete academic disciplines within pharmacy education (e.g., pharmacology, medicinal chemistry, pharmaceutics, pharmacy administration, pharmacy practice), or the curricular material may be integrated across disciplines. Courses are often designed to transform the student from a dependent to an independent learner so that the graduate is prepared for continuous lifelong learning throughout their career.

The focus of laboratory courses is to develop students' skills in various areas of pharmacy practice. In labs, students practice dosage form preparation and administration, product selection, medication dispensing, patient counseling, physical assessment, and other components of delivering pharmaceutical care. Laboratory experiences may be components of didactic courses or may exist as stand-alone courses.

The experiential portion of the curriculum combines the student's knowledge and skills to enable the student to provide actual care to patients and their caregivers, as well as to interact with other healthcare providers. Experiential training is provided throughout all 4 years of the

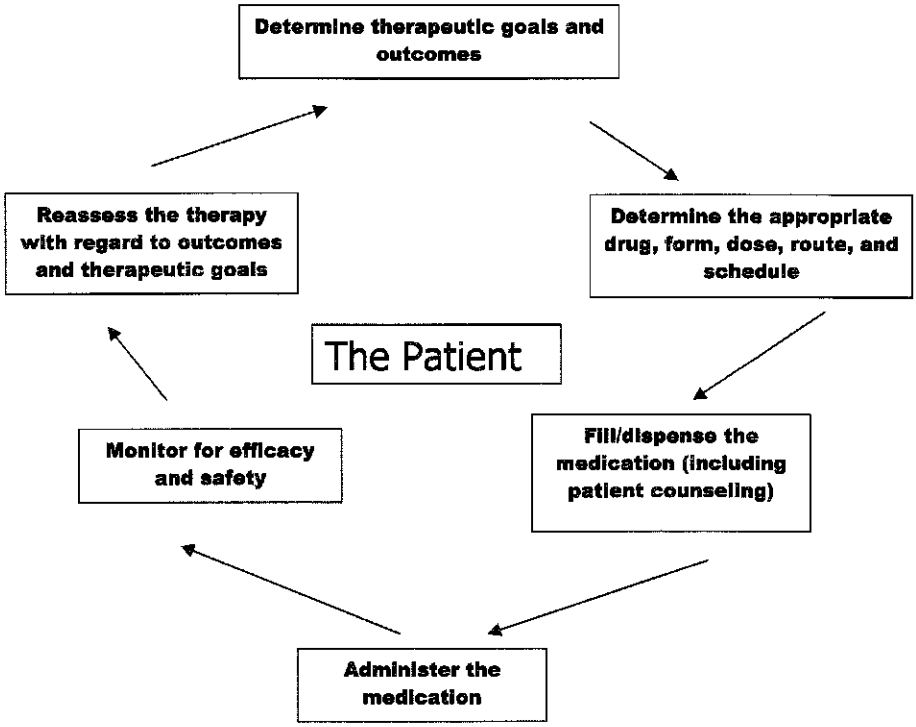

Fig. 1 The process of providing pharmaceutical care.

professional curriculum. Experiences that are taught earlier in the curriculum are usually brief in nature and are designed to introduce students to the healthcare system in general, to the pharmacy profession, or to various aspects of patient care through a combination of observation and participation. The later experiences consist of rotations of several weeks in length through various aspects of pharmacy practice in which students spend all their time learning to manage the practice setting, interacting with other healthcare professionals, and providing direct care to patients. Each rotation may typically last several weeks and include experiences in outpatient and inpatient settings, managed care organizations, pharmacy associations, or the pharmaceutical industry. These advanced rotations are considered capstone courses in which students, through direct practice experience, develop their competence and confidence to practice pharmacy.

CAREER OPPORTUNITIES

There are literally hundreds of different career opportunities for pharmacy graduates. The majority of graduates are employed in traditional community and hospital pharmacies. Many pharmacists, however, seek employment in other patient care areas, including nutritional support, ambulatory care, primary care, pharmacokinetics, pediatrics, and a variety of medical subspecialty areas (e.g., oncology, nephrology, pulmonology, hematology, critical care, infectious disease, emergency medicine, gastroenterology, psychiatry, cardiology). Pharmacists may work in areas of less direct patient care, such as nuclear medicine, drug information, or medical writing. They may be employed in all aspects of managed care, including pharmacy benefits management or formulary development and control, as well as in patient care areas. Pharmaceutical companies employ pharmacists to manage clinical trials, serve as medical liaisons to physicians and other healthcare providers, or work in pharmaceutical sales. There are also careers in academic fields to teach pharmacy students and students in other health disciplines and to conduct research or serve as role models in providing healthcare to patients.

Some career opportunities require additional training or credentialing through residencies, fellowships, certificate programs, and credentialing examinations. Residencies provide intense 1- to 2-year learning opportunities for

continued development of patient care and managerial skills. Fellowships develop pharmacists' research skills to prepare them for careers in the pharmaceutical industry or academia. Credentialing and certification provide specialized training in distinct areas such as nuclear pharmacy and disease management, and may be beneficial to the pharmacist to receive reimbursement for providing these specialized services.

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Drug Enforcement Agency

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INTRODUCTION

The Drug Enforcement Administration (DEA), an organization of the U.S. Department of Justice, is a federal agency whose mission is to enforce U.S. controlled substances laws and regulations and bring violators of these laws to the criminal justice system. The DEA maintains 78 offices in 56 countries throughout the world. Table 1 lists contact information for the DEA.

The DEA has several missions. First, the DEA enforces U.S. controlled substances laws as they pertain to the manufacture, distribution, and dispensing of controlled substances. Second, the DEA investigates and prepares for prosecution organizations and principal members of organizations involved in the growing, manufacture, or distribution of controlled substances for illicit traffic. Third, the DEA liaises with the United Nations, Interpol, and other organizations to reduce the availability of illicit controlled substances, both domestically and internationally.

HISTORY

In 1973, under the administration of President Richard Nixon, several federal drug agencies of various departments of the U.S. government united to form the DEA. The DEA predecessor agencies included the Bureau of Narcotics and Dangerous Drugs, the Office of Drug Abuse Law Enforcement, the Office of National Narcotics Intelligence, the Narcotics Advance Research Management Team, and the Drug Investigations division of U.S. Customs.

DEA PROGRAMS

The DEA operates many programs in an effort to fight the battle of illegal drug use (Table 2). Currently, two major drug threats in the United States are heroin and methamphetamine. More recently, the DEA successfully concluded several operations to address the drug problem in the United States. Operation Tar Pit, for example, successfully targeted a Mexico-based black tar heroin

Table 1 DEA contact information

Type of assistance needed	Contact information
DEA web site	www.usdoj.gov/dea
General comments or questions	DEA Information Services Section; 700 Army Navy Drive; Arlington, Virginia 22202
Physician registration or the Controlled Substances Act	DEA Office of Diversion Control; 600 Army Navy Drive; Arlington, Virginia 22202

Key: DEA, Drug Enforcement Administration.

Table 2 Select DEA programs

Program	Description
Asset Forfeiture	Executes forfeiture of profits and proceeds of designated crimes or property used in drug trafficking crimes
Diversion Control	Prohibits diversion of licit controlled substances and diversion of controlled chemicals into illegal trade
Intelligence	Collects, analyzes, and disseminates drug-related intelligence information in coordination with other law enforcement organizations
Laboratories	Provide forensic drug analysis to law enforcement agencies
Organized Crime Drug Enforcement Task Forces	Fight organized crime and drug traffickers
Marijuana Eradication Program	Funds cannabis eradication program in the United States

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trafficking organization. Another operation, Operation Green Air, successfully halted marijuana trafficking activities of an organization that exclusively used a commercial shipment company, FedEx, to transport the drug. Two additional problems for which the DEA is responsible are the diversion of controlled pharmaceuticals and the diversion of controlled chemicals.

INTERFACE WITH CLINICAL PHARMACY PRACTICE

Although intended for legitimate medical use, narcotics, stimulants, and depressants are frequently abused; therefore, controls have been established by the DEA to prevent their illegal distribution. Registration with the DEA is required of all health professionals entitled to dispense, administer, or prescribe controlled substances and of all pharmacies dispensing controlled substances. Strict regulatory standards relating to drug security and records accountability are required of these groups. Clinical pharmacists should be aware of the potential for drug diversion and be alert to the various ways individuals divert controlled substances. Examples of drug diversion schemes include physicians who sell prescriptions to drug dealers or abusers, pharmacists or nurses who falsify records to steal drugs to sell, employees who steals narcotics from inventory, prescription forgers, patients who obtain controlled substances from multiple physicians, and individuals who falsify narcotic orders to hide illicit sales. Research studies involving controlled substances or investigational controlled substances are subject to strict accountability per DEA regulations.

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Drug History

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INTRODUCTION

Performing a patient drug history involves gathering detailed patient medication information and is an important component of the patient's medical history. The patient drug history provides a thorough understanding of the patient's medication experience, with an emphasis on patient's current medications. The goals of the history are to obtain information on: 1) prescription and nonprescription medications (including dose, frequency, route, indication, and length of therapy); 2) perceived benefit or adverse effects of the therapy; and 3) medication allergies or intolerance. The pharmacist can identify potential medication problems by conducting the drug history. The need for intervention can then be discussed with the health care providers and physicians involved with that patient's care.[1]

Patient Drug History Versus Patient Medical History

The patient drug history focuses on medication therapy and is part of the patient medical history. The medical history encompasses information regarding: 1) past medical and surgical history; 2) acute and chronic medical problems; 3) social and family history; 4) other relevant health information; and 5) the drug history.[1] Depending on the setting, the pharmacist may incorporate elements of the medical history with the drug history. These elements can be used to develop a more thorough assessment and pharmaceutical care plan.

The practice setting and type of patient information available to the practitioner will largely determine the extent and scope of the patient history. Better patient outcomes are ensured by having adequate knowledge about patient's medical problems.[2]

Rationale for a Pharmacist-Conducted Patient Drug History

Traditionally, the physician completes the patient drug history. The physician takes the drug history as part of the medical history in the office or clinic, or upon admission in an acute care setting. Doctors often rely on hospital records, referral letters, or office records as the primary source of information regarding patient drug treatment. Many studies agree that physician histories are lacking, and show that pharmacists' drug histories are more accurate and complete.[3–5] One study documented that 11% of pharmacist-conducted histories contained important clinical information overlooked by the physician.[4] Pharmacists have been involved in obtaining patient drug histories in retail, ambulatory clinic, acute care, and long-term care settings.[3] Pharmacists improve the care provided to patients by becoming involved with the patient history process in their practice setting.

Patient Data Records

The records kept on the patient drug history need to be tailored to the setting. Some patient histories may be a permanent part of a medical record for one individual admission to the hospital, whereas other histories may be part of a continuum of the patient care (e.g., anticoagulation clinic). Records may be stored in a computer database and updated as patients return for follow-up in that care setting (e.g., retail/clinic pharmacy setting). Various forms have been used for record keeping both in written and in computer software formats.

TYPES OF DATA

Subjective Data

There are two ways to classify the types of data collected—subjective and objective. Subjective data refer to all information provided by the patient that cannot be confirmed independently.[1] The weakness of subjective data is that it cannot be confirmed, observed, or measured by the interviewer. However, it can be validated by other means. For example, patient compliance with a medication regimen can be supported by talking with a family caregiver; however, this is also subjective.

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Objective Data

These data are measurable or can be observed. Laboratory values and vital signs such as blood pressure are examples of objective data.[2] Objective data are not influenced by opinion or perception of the patient. Objective data are not infallible and can be limited. For example, if a patient has their blood level checked for drug therapy management, a laboratory error can occur. Objective data such as pharmacy refill records can be used to verify subjective patient information.

SOURCES OF PATIENT DATA

Patients

The patient is the most important source of information regarding their medication therapy. Although the data from the patient is subjective, the interview process can provide clarification on medications taken, knowledge of therapy, and barriers to education or compliance.

Medical Records

The medical record is another source of medication and health-related information. Access to this record may be limited in certain practice settings; however, it can be a valuable tool to review prior to conducting your patient drug history interview. Some practitioners use medical release forms to obtain medical record information such as laboratory data from other institutions required for drug therapy monitoring.[2]

Pharmacy Dispensing Records

Pharmacy refill records can be a valuable source for assessing what the patient is prescribed and how often the patient refills the prescriptions. Clarification of medication usage should be verified by refill records in your practice setting or by contacting pharmacies that the patient uses. Inpatient pharmacists can provide valuable patient information to the outpatient or retail pharmacists upon hospital discharge. This can prevent duplication and medication errors.[5]

Healthcare Providers

Other sources of information regarding medications/therapy can be obtained from home healthcare providers, long-term care facilities, and physician's offices.[5]

Caregiver/Family Member

Many patients rely on a caregiver or family member to assist them with their medications. These individuals can be a valuable source for patient drug history data.[5]

INTERVIEWING THE PATIENT

Setting

The location of the interview should be in a quiet environment free of distractions and allowing patient privacy. Avoid barriers between you and the patient. Respect patient privacy, and discuss the patient's health issues only with those directly involved with the patient's care.[2,5]

Communication

Introduce yourself initially, and describe your intentions and role in the patient's care. Always maintain good eye contact and avoid negative body language. For example, crossed arms or negative facial expressions will not make the patient feel at ease. It is important to record the history data; however, do not let your record taking distract from listening to the patient. Maintaining the continuity of the interview and listening are key to developing the patient's trust.[2]

The history is often affected simply by the way in which we ask the patient about their health problems and medications. Using open-ended questions (i.e., cannot be answered as "yes" or "no") versus closed-ended questions will require the patient to explain and inform you about their therapy. Open-ended questioning helps the practitioner quickly assess the depth of the patient's knowledge about their therapy and health.[1]

The basic format of the history interview will apply to all settings, including acute care, long-term care, ambulatory care, and retail, and can be adjusted to the specific needs of that setting. Utilization of patient data collection forms may be useful for documentation purposes and for guiding the flow and consistency of the interview. There are many sources for the format of data collection forms, which are discussed in a later section.[2,5]

Considerations in Special Patient Populations

"As people develop, have families, and age they provide you with special opportunities and require certain

adaptations in interviewing style."[6] In general, open the interview with the focus being on the patient (ask about school, friends, hobbies, work, family, etc.) to show interest in them personally. Once interest in "them" is established, the patient will usually open up to questioning.[6]

Infants and children younger than 5 years of age: Interviewing the parent will be required, but with the infant or child present. It is always best to refer to the infant/child by name and to the parent by "Mr." or "Mrs." to show both interest and respect.

The information obtained from the parent is third party, but is fairly accurate. Of note, however, the parent may have preconceived ideas about the nature of the child's problem. Practitioners must remember to be supportive rather than judgmental when interviewing the parent of the child. Avoid questions such as "why did you give the child that medicine?" This would imply judgment and that the parent did not have the child's best interest in mind.[6]

Children older than 5 years of age: Avoid talking "down" to children, but rather speak to them normally. The child can be interviewed about their health and medications, both with and without the parent present. First, ask the basic past medical history questions of the parent, then ask to speak to the child alone. Often, the child can tell you in more detail the severity of a problem or perception of medication treatment benefit than the parent.[6]

Adolescents: This population can be difficult to question at times. It is best to be straight forward, and "real" with this age group.

Aging patients: These patients can be visually or hearing impaired, have poor memory, or be slow to answer questions. Be sure to speak slowly and in a lower voice, and give extra time for a response to your questions. Most elderly patients may not be at ease with their medical problems, so be sensitive to them and really "listen." Interview the patient in a comfortable setting free of noise and barriers. If the patient is cognitively impaired, you may have the caregiver and the patient present together. Remember to include the patient in the discussion by acknowledging them and establishing a relationship with them, even if the care provider has to answer questions regarding medication administration, etc.[6]

Language barriers: An interpreter may be needed in special situations. Many pharmaceutical companies provide medication literature in other languages that may be beneficial to have when counseling patients that do not speak the same language.

COMPONENTS OF A PATIENT DRUG HISTORY

Demographic and Patient Financial/ Insurance Information

This section of the history should include the patient's age, date and place of birth, any nicknames, names of both parents, work contact information, gender, ethnicity, address, phone, emergency contact information, names of the pharmacy the patient uses, and insurance information.[5]

Most patients are used to providing this type of information for their doctor's office visits, but may question the pharmacist's need to inquire. The pharmacist should explain that updated information will assist in providing better care for the patient. For example, when a patient's insurance does not cover the medication the patient was prescribed upon hospital discharge, the cost may prevent the patient from taking the medication. Obtaining insurance information prior to patient discharge as part of the history can prevent this type of problem.

Medication Allergies and Intolerances

A medication allergy is a hypersensitivy reaction to the allergen (drug) that provokes characteristic symptoms (rash, urticaria, bronchospasm, or dermatitis) upon subsequent exposure. A medication allergy may be delayed or not seen with initial administration, but after repeated exposure and antibody development the reaction occurs. A drug intolerance is different in that the reaction is not due to an antibody/hypersensitivity response. Intolerance is the inability of the patient to tolerate the particular medication due to a side effect of the medication.[6] Examples of drug intolerance are nausea from codeine or constipation related to an antihypertensive medication. Ask the patient to describe any drug allergies or intolerances using open-ended questions when possible so that they can describe the reaction rather than simply answering with "yes" or "no" to a question. Patients can often confuse medication intolerance with an allergy. The pharmacist can be valuable in clarifying this for the patient record. The information should be as specific as possible, including the description, treatment, and date of

the intolerance/allergy. For infants, children, and adolescent, patients give primary attention to any allergies prevalent during infancy or childhood.[6]

Immunizations

Immunization status is an important part of the medical history. Recording dates of childhood immunizations is pertinent so that ongoing boosters can be scheduled throughout childhood and adolescence.[6]

Adult immunizations are important to document as well and include vaccines such as pneumococcusl (for elderly and those at risk for pneumonia), influenza, hepatitis B, and tetanus. Although not an immunization, skin testing for tuberculosis might also be included under this section in high-risk patients (elderly, health care worker, or immunocompromised patient).

Medications

This list should include all prescription and nonprescription medications (including nutritional supplements, vitamins, and herbal remedies) the patient is taking. Information regarding the dosage strength, frequency, length of therapy, indication for use, and adherence must be obtained. Perceived benefit from the medication or any adverse experiences due to the medication should also be noted. Remember to inquire using open-ended questioning with patients using words such as "how," "what," and "when."[1,2,5]

Examples of open-ended questioning are "What are you taking this medication for?", "How do you take your medication?", and "What do you do when you miss a dose of your medication?" Closed-ended questions will not really tell the interviewer how much the patient understands about the dosing and purpose of medications without further questioning. Avoid questions such as "Do you take all of your medicine once a day?", "Do you miss any doses?", and "Did your doctor tell you what this is for?". All of these questions could be answered with either "yes" or "no," and additional questioning would then be required for clarification. The open-ended style is efficient in that one type of question tells the interviewer all the patient's strong knowledge points and also pinpoints weak areas.[2]

Additional Home Monitoring and Compliance Aids

Establish records on patient use of any monitoring devices (i.e., blood glucose monitor) or compliance aids. This information helps understand the need for additional compliance aids or education on monitoring devices to improve therapy outcomes.[5]

Barriers to Compliance

Barriers to compliance must be identified during the history. Emotions, cognitive function, and physical ability can affect patient adherence to therapy. If a patient suffers from depression (emotional barrier), schizophrenia or dementia (cognitive barrier), or severe arthritis of the hands (physical barrier), compliance can diminish. Special attention should be given to these three areas, and barriers should be indicated on the history record. This process directs the implementation of specific aids to improve compliance.[5]

ADDITIONAL INFORMATION FOR PATIENT HISTORIES

The following sections are typically part of the broader medical history. These sections may be included to provide a more thorough assessment of the patient's therapy and health needs.[1–3,5,6]

Social History

The focus of the history is the patient's occupation, lifestyle, family relationships, and support system. Points of inquiry include job, marital status, diet, social drug use (i.e., alcohol, tobacco, illicit drug use), and religious beliefs related to health care. Asking patients about their use of alcohol and illicit drugs can be difficult for practitioners. It is not our role to pass judgment on the use of these agents, rather it is our job to gather the information to properly assess the patient and their health. Explaining to the patient that health outcomes are often affected by lifestyle choices and the family support for the individual may help with this part of the interview. For example, a visually impaired patient would need assistance with drawing up insulin. The support systems in place to assist the patient with the insulin preparation and administration need to be identified.

Acute and Chronic Medical Problems

Knowledge of the patient's health status will help the practitioner understand the purpose of the prescribed therapy, select optimal therapies for the patient, and help prevent adverse drug–disease state interactions. For example, a pharmacist would want to avoid recommend-

Name: _____ **MR#** _____ **Date:** _____
Age: _____ **Gender:** _____ **Ethnicity:** _____ **R.Ph.:** _____
INSURANCE INFORMATION: _____

PMH (acute/chronic medical problems):

_____

_____

_____

PSH (past surgical history): _____

SH (social history):

___ EtOH ___Tobacco use (amounts)_____
____ illicit drugs (list type if yes)_____
____ job status (list type of work)_____
____ marital status ____children (number)_____

_____

_____

Allergies/Immunizations:

Medication	Type of Reaction	Allergy or Intolerance

Immunizations:

___**Pneumococcal vaccine: (dates)**_____
___**Hepatitis B: (dates)**_____
___**Influenza: (dates)**_____
___**Tetanus: (dates)**_____
___**MMR: (dates)**_____
Other: _____

Prescription Medications	Dose/Frequency	Therapy Dates

Nonprescription Medications	Dose/Frequency	Therapy Dates

Herbal/Nutritional Supplements	Dose/Frequency	Therapy Dates

COMMENTS/ NOTES:

Fig. 1 Patient history form.

ing a nonsteroidal antiinflammatory drug for a patient with a recent gastrointestinal bleed.

Information gathered should include all medical problems the patient receives treatment for such as hypertension and diabetes. Problems the patient has been treated for in the past and past surgical procedures should also be noted. In children, it is important to include childhood illnesses (i.e., mumps, chicken pox) and exposure to these as well.

The medications prescribed will help prompt the interviewer to ask about specific medical problems such as antihypertensives being prescribed for the patient who has hypertension. Open-ended questions help the interviewer to become the listener and the patient to become the information provider.

USE OF DATA COLLECTION FORMS

Specific forms for patient drug histories are not required, but may benefit the history-taking process. The advantages of a patient drug history data collection form are: 1) it establishes a record (written or computerized) for the pharmacist's future use; 2) it provides a format for prompting questions during the interview; 3) its consistent format fosters organized flow of questioning; and 4) it prevents duplication of questioning in the future. The data recording process should never detract from the interaction with the patient.

The format can vary, but most forms will contain lines, tables, or checklists for the patient history components discussed in this entry: demographics, social information, allergy information, medical problems and procedures, and patient prescription and nonprescription medications.

Many sources have good examples of patient data collection forms.[2,5] An example of a patient history form is given in Fig. 1. The format of the form will require modification for the specific care setting and goals of the individual practitioner.

Some drug therapy management clinics use computer databases that store the patient history information and can print out the profiles when needed.[8–10] A few examples of data management software programs include CoumaCare® Patient management system, Anticoagulation Management Program (AMP) Anticoagulation, and Information Manager (AIM).[7–9] Pharmacist-managed anticoagulation and lipid clinics often use software programs to store and update patient history information.

MORE INFORMATION

Some key web sites to visit to obtain additional information on patient history taking as related to pharmaceutical care practice would be www.ashp.org (under practice standards or primary/ambulatory care), www.aphanet.org (under pharmaceutical care), www.auburn.edu (under case presentation guidelines), and www.altimed.com (under focus on patient communication). Medical-affiliated web sites that have some information on patient histories are www.ama-assn.org, www.acponline.org, and www.med.stanford.edu (under shs/smg/tools for pt. History forms). A web site for interpreter-guided interviews is www.hslib.washington.edu (under/clinical/ethnomed/intrprt). For more in-depth discussion, three referenced publications provide an excellent review on conducting patient medical and drug histories.[1,2,5]

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PROFESSIONAL DEVELOPMENT

Drug Information Pharmacy Practice

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INTRODUCTION

Drug information is an area of pharmacy practice that deals with obtaining, managing, and evaluating information to prepare and disseminate it in a suitable format, wherever and whenever it is needed or in anticipation of need. This area of practice is one of the oldest in clinical pharmacy, with the decision to establish a drug information center being made in 1959 at Ohio State University[1] and 1960 at the University of Kentucky,[2] with the latter one being the first to open in 1962.[3] The drug information specialist has not specifically been considered a documentation specialist, as is a librarian, but was originally defined as a subject-oriented specialist in the area of drug knowledge.[4] Usually, this definition is broadened to include both pharmaceutical and therapeutic knowledge,[1] which has lead to controversy over the true name for the area of practice.

Usually, the term *drug information* is coupled with terms such as *specialist*, *center*, or *service*. Some people have substituted the words *medication* or *biomedical* for *drug*, due to the negative connotation that the latter term has in society. Others have substituted the word *informatics* for *information*, to better acknowledge the increased role of computers in information management. Unfortunately, a better term or phrase that indicates that people working in this area deal with information relating both to drugs (e.g., therapeutics, adverse drug reactions) and to pharmacy (e.g., how to perform various pharmacy tasks) has not been identified.

Individuals working in the area of drug information possess some of the skills of a documentation specialist because these skills are necessary to manage information. However, unlike pure documentation specialists, the drug information practitioner has the ability to adequately understand the initial problem and, after locating the information using the skills of documentation specialists, can evaluate the information and use it to formulate a solution to a particular pharmacy or medication-related situation. Because of this ability, drug information practitioners have occasionally been referred to as the "ultimate generalist" in pharmacy. They do not necessarily know the in depth information that a specialist in a particular clinical or practice area would have about that particular specialty, but the drug information practitioner has the in depth knowledge of how to obtain the necessary information and use it to address specific problems or concerns in most areas.

The need for drug information practitioners is likely to increase due to the rapid increases and improvements in information and the technology to manage it, particularly due to Internet technology and information sources. Skills expected of drug information practitioners in the 1980s are now expected of many pharmacists; drug information practitioners now are expected to have even greater skills, and the ability to handle larger and more complex information management situations.

CLINICAL PHARMACY OPPORTUNITIES

It is difficult to describe clinical pharmacy opportunities in relation to drug information because drug information skills are at the core of clinical pharmacy practice. It is impossible for anyone to know everything they need to know about pharmacy practice, and new information is becoming available so rapidly, particularly with the advent of the Internet, that even adequately keeping up with methods of obtaining and managing information is difficult. Given that, it can be stated that in any pharmacy environment there are opportunities for individuals who specialize in information management, whether that be in community, institutional, academic, industry, managed care (including health maintenance organizations and pharmacy benefit managers), insurance companies, associations, government, or other environments.

MODEL CLINICAL PRACTICES

Community

Few community pharmacy-based drug information practices have ever existed. Occasionally, however, there have

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been such practices to provide information to patients. These were sometimes established using grant funding, but failed financially afterward. There have been some practices for a fee (e.g., 900 phone numbers), with good results. Now, more drug information is being provided via the Internet. This includes services such as those run by Internet pharmacies (e.g., http://www.rx.com), pharmacy organizations (e.g., http://www.pharmacyandyou.org), and even individual pharmacists (e.g., http://www.medconsultant.com/index.shtml).

Functions of those services tend to center around providing prepared drug information documents (e.g., patient information sheets) and answering specific medication-related questions. These are seldom money-making operations, but are often provided as a service to attract customers to a pharmacy or as a public service.

Institutional and Academic Practice

These two environments are grouped because they are similar in nature and are often combined. Typically, practitioners here are located in a dedicated drug information center that resides in a hospital pharmacy or medical library. Typically, such services were begun to provide literature searches and answers for specific questions and to perform formulary management.[5] Given the greater concern for the cost of services, the former service is now sometimes deemphasized. Instead, services that will decrease hospital costs (including liability), increase income, or provide functions that are required by legal or regulatory bodies are often performed. Overall, it has been shown that having a drug information service may save 2.9 to 13.2 times its cost.[6]

The following functions are performed by drug information practitioners in the institutional and academic environments:[7]

- Answer questions and perform literature searches.
- Drug formulary management (e.g., evaluating drugs for addition or deletion from the formulary, preparing use guidelines and policies and procedures, pharmacoeconomic analysis), including publication of a drug formulary book, whether in hard copy or electronic format.
- Quality assurance activities (e.g., departmental quality assurance, drug usage evaluation, medication usage evaluation). This includes setting up, managing, and evaluating the data from such activities.
- Development and/or modification of evidence-based clinical guidelines. This includes the concepts of disease state management and outcomes management.
- Development and/or modification of policies and procedures.
- Adverse drug reaction/medication error tracking and reporting.
- Investigational drug information (e.g., Institutional Review Board activities, central depository of study protocols, providing patients and practitioners with information about investigational drugs, managing medication studies).
- Poison information—occasionally, drug information services are run in conjunction with poison information services.
- Management of department information equipment, software, and procedures.
- Provision of educational programs and materials, which may include newsletters and web sites.
- Potential contract services with industry, managed care, or insurance companies and other groups to provide specific information services (see the information listed under those environments for further information on necessary services).[8]
- A major function for academic, and occasionally institutional, drug information centers is education. This can include pharmacy students, residents (general or drug information specialty residents), and fellows.

Drug information practitioners in institutional and academic environments may work within a single institution or may be involved in a hospital system that requires services to multiple institutions, perhaps over a wide geographic region.

Industry

Within the pharmaceutical industry there is a major need for drug information specialists for a variety of functions:

- Answering information requests from health care professionals, employees, and occasionally patients.
- Preparation and management of information databases for employees.
- Preparation of materials to be distributed directly to health care professionals, employees, and patients.
- Setting up and managing clinical drug research and the information derived from it.
- Preparing Food and Drug Administration (FDA)-required information, such as New Drug Applications.
- Collecting, collating, and using adverse drug reaction information.
- Provision of training to pharmacy students and residents.

It is important to note that in the industrial environment, physicians often manage the drug information services or other areas that use drug information practitioners, while they are staffed by some combination of physicians, pharmacists, nurses, or others.

Managed Care and Insurance Companies[9]

Drug information services in a managed care or insurance company environment often deal with issues concerning providing the lowest cost therapy for patients (i.e., keeping reimbursement cost low). At one time, this might have amounted to individuals (including nonpharmacists) simply reviewing and comparing the costs of drugs within a therapeutic class. The assumption was that they were all interchangeable. Fortunately, it has become more widely recognized that many factors are involved in providing the best and least expensive therapy to patients. This includes the efficacy of the drug, adverse effect frequency and severity, cost of monitoring, the need for additional care, the length of therapy, and a variety of other therapeutic, ethical, legal, and patient issues. A full pharmacoeconomic analysis is necessary to ensure that all aspects are evaluated. It is not unusual that a drug product that initially looks to be the least expensive may actually be the most expensive due to a variety of reasons, such as a need for increased monitoring, lower efficacy, more severe adverse effects, etc. Drug information centers may evaluate whether reimbursement is available for drugs or the disease state, what copays might be required, restrictions or authorizations that are needed before medication use, and other information.

Also, drug information centers in these environments may spend a lot of time preparing information on the best way to treat disease states to produce optimal outcomes for the lowest cost (i.e., disease state management, outcomes management). This information may be used either actively or passively to educate health care practitioners, particularly physicians and pharmacists.

Drug information practitioners in these areas may also perform other drug information activities, such as answering questions, quality assurance, and electronic information interchange on a national level. Other activities listed under institutional practice may also be carried out.

Associations

Various professional associations have drug information needs. This may have to do with association publications; researching items of interest to the association; providing information for association members or other interested people; and preparation of statements, guidelines (including evidence-based, clinical guidelines), and other official documents.

Government

Government organizations at the national or state levels have a need for drug information specialists. For example, FDA (http://www.fda.gov) can use the services of drug information practitioners in the collection, organization, management, and distribution of information on drugs (both investigational and marketed).

At a state level, drug information practitioners may be involved with drug utilization review, whereby data on drug usage patterns is collected and analyzed to determine ways by which drug therapy may be improved.

Other activities similar to those listed for managed care organizations can also be performed by government drug information practitioners. Also, some state and foreign governments have drug formularies, which drug information practitioners would be involved in managing.

MATERIALS USEFUL FOR DRUG INFORMATION PRACTITIONERS

There are a variety of resources that may be of value to drug information practitioners, both in learning how to perform the various necessary skills and in carrying out the responsibilities.

There is currently one general reference to guide drug information practitioners and those who would like to learn the skills. Other general references are currently out of print, although some may still be obtainable. They are as follows:

- Malone PM, Mosdell KW, Kier KL, Stanovich JE. *Drug Information—A Guide for Pharmacists*, 2nd ed. New York: McGraw-Hill, 2001. This is the most complete and up-to-date reference, covering all aspects of drug information practice, including formulary management and quality assurance. It includes extensive lists of references and Internet sites that are of use to individuals who are trying to obtain drug information. Also, this reference covers the evaluation of all types of literature, rather than just clinical studies, which many other drug information books are limited to covering.

The June and August 1998 issues of *Journal of Pharmacy Practice* are also devoted to the practice of drug information and contain a great deal of useful

information, similar to the contents of the previously mentioned books.

There are also references that cover specific aspects of drug information practice:

- Galt KA. *Analyzing and Recording a Drug Information Request*. Bethesda, MD: American Society of Hospital Pharmacists, Inc., 1994. This first module in a series of three deals with the skills needed to initially take a drug information request, mostly from a general practitioner's point of view.
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- Galt KA, Calis KA, Turcasso NM. *Preparing a Drug Information Response*. Bethesda, MD: American Society of Health-System Pharmacists, Inc., 1995. This third module takes the information obtained and evaluated using methods in the first two books and describes methods to effectively distribute it. Again, it addresses the subject from the point of view of the average pharmacy practitioner.
- Ascione FJ. *Principles of Scientific Literature Evaluation: Critiquing Clinical Drug Trials*. Washington, DC: American Pharmaceutical Association, 2001. While previous editions of this book were somewhat broader in scope, the current edition specifically covers the evaluation and interpretation of scientific papers describing clinical trials.
- Slaughter RL, Edwards DJ. *Evaluating Drug Literature—A Statistical Approach*. New York: McGraw-Hill, 2001. This book covers a wider area of drug literature evaluation than the previous reference, including some information on other topics, such as performing a literature search.
- Snow B. *Drug Information—A Guide to Current Resources*. Lanham, MD: Scarecrow Press, Inc., 1999. This is an extremely comprehensive book that lists and describes multiple sources of drug information. The focus is very limited, but no other book covers this subject as completely.

There are many resources available to the drug information practitioner. They will not be presented here due to their vast number, but they are described in some of the previous references. It should be noted that many of those resources are now available electronically (e.g., evidence-based clinical practice guidelines are available at http://www.guideline.gov), allowing wider access and easier use. Also, references dealing with the electronic management of information are particularly helpful to drug information practitioners.

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PROFESSIONAL NETWORK OPPORTUNITIES

There are a variety of professional networking opportunities available through professional associations for drug information practitioners. They are presented here in alphabetical order:

- *American Medical Informatics Association (AMIA)*—This group is concerned with health information technology. It consists of members in a wide variety of professional areas. Some professions, such as dentists and nurses, have specific working groups in the association. Some drug information pharmacists are members, but there is not yet a working group for those individuals. Further information about this organization can be found at http://www.amia.org.
- *American Society of Health-System Pharmacists (ASHP)—Clinical Practice Section—Drug Information/Pharmacoeconomics Network*—Members of ASHP can also become members of the Clinical Practice Section, which has many practitioner networks. One of these is for drug information and pharmacoeconomics. This network sponsors continuing education programs at the ASHP annual and midyear clinical meetings. Members are also provided a time and place to gather at the midyear clinical meeting, and sometimes the annual meeting, to discuss topics in their area of interest. In addition, an e-mail listserve is available for communications among members of this network and information is available for members at http://www.ashp.org/clinical/index.html. This group would be of most interest to institutional and academic drug information practitioners. A variety of guidelines, as well as position statements of interest to drug information practitioners on such subjects as formulary management and medication use evaluation, are available at http://www.ashp.org/bestpractices/index.html.
- *Consortium for the Advancement of Information, Policy and Research (CAMIPR)*—This is the newest of the drug information associations, formed in 1994 to better serve the needs of institutional and academic drug information pharmacists.[10] This group generally meets in conjunction with the ASHP midyear clinical meeting. There is no cost involved in joining the organization; it is only necessary to join their listserve. Information on joining and compilations of previous

listserve discussions is available at http://druginfo.creighton.edu/camipr.

- *Drug Information Association (DIA)*—The DIA is a group devoted entirely to drug information specialists, including physicians, pharmacists, and others. It is mostly involved with drug information practitioners in industry practice. Information on the organization and its services can be found at http://www.diahome.org.

Other smaller drug information groups also exist.[11]

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Drug Samples

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INTRODUCTION

Drug sampling is an important, although controversial, marketing technique used by pharmaceutical companies. Over half of the $13.9 billion spent in 1999 on the marketing of prescription drugs by pharmaceutical companies was for "free" medication samples.[1]

Drug sample availability is intended to increase market share of products by directly influencing providers' prescribing habits. Sampling also opens doors for pharmaceutical representatives to gain access to busy prescribers. Sampling gives representatives a reason to visit prescribers' offices and provides prescribers an incentive to permit representatives to visit. The influence of pharmaceutical representatives on physician behavior is well established.[2]

Inventories of drug samples valued at tens of thousands of dollars fill closets and even entire rooms of many outpatient clinics, physician offices, and emergency rooms.[3–6] Reports suggest that prescribers dispense samples at 10–20% of patient encounters, although there is wide variation between and among practices.[3,5] The most commonly dispensed samples in primary care settings include pulmonary medications, anti-infective agents, analgesics and anti-inflammatory drugs, allergy medications, cardiovascular agents, gastrointestinal agents, and oral contraceptives.[3–5]

REGULATORY ISSUES

Before the implementation of the Prescription Drug Marketing Act (PDMA) of 1987, record keeping of sample distribution was not required.[7,8] Abuses in the system of distributing samples that "resulted in the sale to consumers of misbranded, expired, and adulterated pharmaceuticals" led to the passage of the PDMA.[8] The PDMA prohibits the selling of samples. The Act requires signed requests for samples by practitioners licensed to prescribe such drugs. The PDMA includes provisions to the manufacturer on record keeping and reporting to the Food and Drug Administration. It also requires storage conditions that maintain the stability, integrity, and effectiveness of sample products and keep products free of contamination and deterioration.[8] Because state laws and regulations on samples vary, Boards of Pharmacy should be contacted for state-specific information.

Clinics and emergency rooms of hospitals and health systems must follow standards set by the Joint Commission on the Accreditation of Healthcare Organizations (JCAHO) for sampling and medication use. JCAHO requires policy and procedures related to the control of drug samples.[9] In addition, all other JCAHO standards that are applicable to medication use, including uniformity in processes, apply to drug samples to the same extent as they apply to regular prescription medications dispensed by the hospital pharmacy.[9] Specific methods or processes for controlling samples are not dictated by JCAHO, although certain features of the sampling system may be inspected[9] (Table 1).

BENEFITS

The availability of drug samples can benefit prescribers and patients. Prescribers often report using drug samples to avoid medication costs to the patient.[5,10,11] Samples may be used before a full prescription is purchased so that safety, tolerability, and effectiveness can be evaluated, or doses titrated.[11,12] Samples may be used to partially or fully offset the cost of drugs for indigent patients or to avoid formulary restrictions or prior authorization requests.[5,10,11] Prescribers may use samples to initiate therapy immediately in the office, allowing patients to avoid a trip to the pharmacy. This may be important for urgent and painful conditions, and for after-hours care.[11] Samples can be helpful for demonstrating appropriate use of inhalers, topical products, and other medications.[13] Prescribers frequently report that sampling is beneficial, because it allows them to gain experience with new

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Table 1 Criteria JCAHO surveyors generally look for in evaluating compliance

- There is a system, defined by policy and procedure, for the control, accountability, and security of all drug samples throughout the organization.
- The drug samples are properly stored.
- Drug sample storage areas are routinely inspected.
- Drug samples are secure.
- Drug samples are labeled and dispensed according to the same standardized method that the hospital uses for nonsample prescription medications.
- Documentation requirements for sample drugs should be the same as other nonsample medications ordered and dispensed by the clinic or hospital.
- There must be an effective recall mechanism for drug samples.

(From Ref. [8].)

drugs.[11] Other factors for dispensing samples include improving patient satisfaction and adherence.[10,14]

CONCERNS

Despite the many apparent benefits of sampling, the practice has been heavily criticized. Concerns surrounding sampling include patient safety, product integrity, security and control of samples, ethical issues, influence on prescribing habits, and costs to the healthcare system.[3,5,9,10,15–24]

Important safety controls are lost when samples are used. Sampling bypasses the safeguards of pharmacist medication regimen review and counseling. Drug interactions, which are screened when prescriptions are dispensed at pharmacies, may go undetected when samples are used.[15,16] Labeling samples with patients' names and instructions for use is often inconsistent, if it is done at all.[3,5,10,16] One study found that instructions to the patient accompanied less than 50% of patient encounters involving sample dispensing and were predominantly verbal in nature.[3] Patient information sheets are infrequently provided by the manufacturer in sample packaging, and most providers do not have systems to generate the extensive printed information that is provided to patients at pharmacies.[17] There is also concern about increasing prescribing errors, because formulary and nonformulary drugs with which prescribers and staff may not be familiar are often delivered by representatives.[16]

The potential for inadequate sample inventory management in prescribers' offices and inappropriate storage of products by pharmaceutical representatives raises concern about product potency and stability. Expiration dates and product recalls may go unnoticed.[15,16] Products might be stored in garages and automobile trunks of pharmaceutical representatives, potentially exposing samples to extremes in temperatures or humidity.

Significant deficiencies in the security and control of samples have been well documented.[5,18–21] In fact, it has been estimated that just over half of samples actually reach patients.[5] Samples may be used by prescribers and staff, or they may be diverted. Personal use of drug samples by physicians and other healthcare providers raises ethical concerns and is not without risk.[18,19] Limaye and Paauw described three medical residents who self-prescribed antimicrobials and were subsequently diagnosed with *Clostridium difficile* infection.[19] Tong and Lien reported self-medication with samples and distribution of samples to nonphysicians by almost 60% of pharmaceutical representatives surveyed at a Canadian family practice office.[20] A contributing factor to some of these issues is that institutional or facility sample policy and procedures are often absent, or compliance is poor. One institution found only 10% compliance when the inventory of samples was compared with the required written documentation. Even after an educational program in which the policy was explained to the house staff, a second audit found only 26% compliance.[21] Poor compliance with policy and procedure may jeopardize patient safety, as well as put the institution at risk for JCAHO recommendations or Board of Pharmacy penalties.

Another concern is that drug choices may be dictated more by what is available in the sample closet than by evidence-based recommendations or by known cost-effectiveness. The influence of sampling has potential implications for patient care and healthcare costs. While studies have shown that sampling may increase subsequent prescription of the sampled drugs, research on the quality of prescribing related to sampling is sparse.[5,9,10] A survey by Chew et al. of physicians' self-reported prescribing patterns for three clinical scenarios found that the availability of drug samples led physicians to dispense and subsequently prescribe drugs that differ from their preferred drug choice.[9] In addition, the study found that when drug samples were made available, 27% of physicians indicated that they would dispense a drug sample not recommended as a first-line agent by the Joint National Committee on Hypertension.[9]

Because sampling is labor intensive and is subject to industry and institutional regulations, it is a very costly practice. In addition to the wholesale value of samples, there are other costs, such as packaging, distribution via representatives, prescriber and staff time interacting with

representatives and handling samples, and institutional administration of sample programs. The bulky cardboard packaging that is characteristic of drug samples not only creates an inordinate amount of waste, it also takes up valuable office space.[22,23] Health systems likely incur the financial burden of giving out "free" samples when less expensive medications are available, although there is little evidence supporting this. A sample is only free in the sense that neither the prescriber nor the patient paid cash for it when it was received.

Despite the many shortcomings of sampling, it is often continued, because it enables prescribers to provide medications to indigent patients. However, sampling is an inefficient method for helping patients in need of medications.[24] Supplies may be inconsistent, and multiple packages of samples are usually required on a frequent basis to maintain patients' needs. Patients often do not get as much drug as needed, or they are switched from brand to brand based on the samples that are available, creating confusion for patients and prescribers.

IMPROVING THE PROCESS

Efforts to address concerns about sampling range from development of policies and guidelines for sample use to restrictions and banning of samples. Pharmacists are involved in, and many times spearheading, sample practice changes.[14,16,21,25–27]

In facilities where samples are used, important first steps to bringing sample practices into compliance include consulting state and federal regulations and JCAHO standards (Table 1). Guidelines and recommendations from organizations such as the Society of Teachers of Family Medicine and the Institute for Safe Medication Practices (ISMP) can be consulted.[16,28]

Other innovative approaches to improve sampling processes have been developed. Multiple-part carbonless adhesive forms with space for patient name, date, medication name and strength, quantity, directions for use, lot number, expiration date, and physician signature have been created for signing out samples. One copy goes to the patient, one goes to the chart, and one is kept for record maintenance. This type of system helps ensure written directions, provides a double check on expiration date, and becomes a log with lot number in the event of a recall. Although it is time-intensive, maintaining a perpetual inventory or auditing closets and sign-in/sign-out logs on a regular basis is a way to determine if samples are being stolen. Posting information about unaccounted for samples may heighten awareness of security and compliance issues.

Some pharmacists dispense samples in the clinic when requested by prescribers. A full range of services, including assisting with product selection, labeling the product, and counseling the patient, may be provided. Sometimes pharmacists supervise nursing staff that order, stock, label, and discard samples.[25] Educational efforts to promote sample compliance and appropriate prescribing are often done or coordinated by pharmacists. Providing reviews and summaries of treatment guidelines and evidenced-based pharmacotherapy that include formulary and cost information to small groups, via newsletters and in postings in sample closets, are common academic detailing activities used to counter sampling practices.

To further encourage prescribing of cost-effective drugs, some clinics request generic samples or prepackaged first-line medications. Generic samples are available from some manufacturers, and at least one pharmacy benefit management company is planning to provide samples of generic drugs in its efforts to encourage the use of generic drugs. Unfortunately, there has been limited success in getting prescribers to use generic samples or prepackaged first-line medications.[21]

Technology is being used to improve sample control and patient safety. Some facilities have developed databases to generate labels and to log lot numbers of samples dispensed. Sophisticated systems that include computer-controlled dispensing cabinets are marketed by companies like www.drugsampling.com. These systems include fingerprint-recognition technology to open the cabinets and touch screen monitors that can be used to generate medication labels, patient education, and required dispensing documentation. The systems are paid for by renting space in the cabinet to drug companies. The value for the manufacturer, according to a company that markets this type of system, is to maintain sampling privileges in clinics where sampling is at risk of being banned because of poor control and to provide sample usage information to the manufacturer.

Restricting samples to drugs available on or preferred by the organization's formulary is an approach used by some organizations to discourage prescribing of nonformulary drugs. Some clinics appoint a committee, which usually includes a pharmacist, to develop a formulary of requested samples based on safety, efficacy, and cost.[16,25] General guidelines that one clinic used in selecting formulary samples included: 1) stocking one or two of the least expensive drugs in each therapeutic class; 2) delaying the addition of new agents until adverse reactions and drug interactions are clinically demonstrated; 3) refraining from adding "me too" drugs unless they have clear advantages; and 4) accepting drugs that

have generic equivalents offering long-term savings to patients.[25] Some clinics simply restrict samples to those that address the most common needs of patients treated in the practice.[25] Placing restrictions on the types and quantities of samples requested promotes efficient use of storage space by reducing the number of unused and expired products.[16,25]

Despite implementing many of the controls mentioned above, more and more facilities are banning samples.[14,21] Most cite concerns about complying with regulations and the promotion of poor prescribing habits that lead to increased costs. Vigilance in enforcing policies prohibiting samples is necessary, because it is likely that samples will find their way into clinics.[16] Interestingly, some institutions provide exemptions from the sample bans when a pharmacist in the clinic is responsible for ensuring compliance.[14]

ALTERNATIVES TO SAMPLES

Coupons or voucher systems have been proposed as an alternative to samples.[14,16] Voucher systems rely on prescribers to issue coupons to patients who then present the coupons along with their prescriptions to the pharmacy of their choice. With the information provided on the voucher, prescriptions are paid for through on-line pharmacy claims. Medications are dispensed to patients fully labeled and with counseling.

Medications for indigent patients may be obtained through pharmaceutical company medication assistance programs.[29] These programs provide brand name medications to patients based on financial need. Each company determines the eligibility criteria for its program. The application processes and the amount of medication supplied vary. While medication assistance programs help thousands of patients obtain medications, it requires cumbersome paperwork and frequent reapplication, and there can be considerable delays in getting medication to patients.[30] Like sampling, medication assistance programs are limited in their ability to help indigent patients.

CONCLUSION

Drug sampling is a controversial marketing technique used to promote pharmaceuticals. Pharmacists should be encouraged to get involved in efforts to promote safe and appropriate use of samples and ensure control and security. Clinics and institutions should have and enforce policies and procedures for managing samples. Controlling which samples will be requested and ensuring appropriate labeling, documentation screening for drug interactions, and patient education will help improve the use of drug samples.

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Economic Evaluations of Clinical Pharmacy Services (ACCP)

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INTRODUCTION

The objectives of this effort were to summarize and critique original economic assessments of clinical pharmacy services published from 1988–1995, and to make recommendations for future work in this area. A literature search was conducted to identify articles that were then blinded and randomly assigned to reviewers to confirm inclusion, abstract information, and assess the quality of study design. The 104 articles fell into four main categories based on type of service described: disease state management (4%), general pharmacotherapeutic monitoring (36%), pharmacokinetic monitoring services (13%), and targeted drug programs (47%). Articles were categorized by type of evaluation; 35% were considered outcome analyses, 32% outcome descriptions, and 18% full economic analyses. A majority (89%) of the studies reviewed described positive financial benefits from the clinical services evaluated; however, many (68%) did not include the input costs of providing the clinical service as part of the evaluation. Studies that were well conducted were most likely to demonstrate positive results. Commonly, results were expressed as net savings or costs avoided for a given time period or per patient. Seven studies expressed results as a benefit : cost ratio (these ranged from 1.08 : 1 to 75.84 : 1, mean 16.70 : 1). Overall, this body of literature contains a wealth of information pertinent to the value of the clinical practice of pharmacy. Future economic evaluations of clinical pharmacy services should incorporate sound study design and evaluate practice in alternative settings.

In 1989, the American College of Clinical Pharmacy (ACCP) published a position statement entitled "Prospectus on the Economic Value of Clinical Pharmacy Services."[1] The document summarized literature published prior to 1988 that supported the economic value of clinical pharmacy services and as such provided a resource to the profession in efforts to advance the clinical practice of pharmacy. A similar review was published in 1986.[2] These papers have proved to be valuable indexes of the literature and have been referred to by many in the profession on points pertinent to the economic value of clinical pharmacy.

In the time that has passed since the original ACCP prospectus, the literature has continued to grow in both depth and breadth of evidence supportive of the financial justification of clinical pharmacy services. New service models and philosophies of practice have developed in the past 6 years, the most notable being that of pharmaceutical care.[3] In addition, our ability to evaluate scientifically and measure the impact of clinical services on costs and outcomes has matured with the increased understanding and use of analytical techniques in health economics and pharmacoeconomics.[4,5] The effect of these advances on the quality and quantity of literature is unknown. The ACCP Board of Regents thus asked the ACCP Publications Committee to update this prospectus.

The committee reviewed, summarized, and critiqued the literature published between January 1988 and December 1995 that included original economic assessment of clinical pharmacy services or programs, thereby serving to update the original position statement of ACCP. Further intentions were to provide a barometer of the degree to which accepted techniques of economic analysis have been incorporated into this literature, and to make recommendations for future work in this area.

METHODS

A search of two major data bases (MEDLINE, International Pharmaceutical Abstracts) was conducted to identify articles published between January 1988 and December 1995. The beginning date of January 1988 was selected because the original ACCP prospectus was inclusive through December 1987. Both MeSH and free text search terms were used to identify English language articles assessing the value of clinical pharmacy services. Search terms were clinical pharmacy services, pharmacy

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services, program, economic evaluation, cost justification, cost, cost effectiveness, cost–benefit, cost analysis, cost–consequence analysis, and cost–utility analysis. Review articles, editorials, and other unoriginal reports were excluded from the search. All citations identified were screened for inclusion by review of titles and abstracts. Those articles for which abstracts were not available from the computerized databases were collected manually and screened for inclusion.

Inclusion criteria were English language, original evaluation, publication between January 1988 and December 1995 inclusive, assessment of a clinical pharmacy service (defined as patient-level interaction, and not including policy-type interventions unless accompanied by a patient-level interaction), and some economic assessment. Exclusion criteria were reviews, editorials, and letters, and studies published in abstract form only. All papers suspected of meeting the inclusion criteria were submitted to full review. In addition, the authors examined personal files, and a secondary search of the titles of articles cited in papers meeting the inclusion criteria was conducted. Papers identified through this search were again collected and screened for inclusion, and added to the set of papers subjected to full review.

In the full review process, a modified block randomization scheme was used to confirm inclusion and to abstract information and assess the quality of each article. Each paper was randomly assigned to two of four reviewers. Reviewers were blinded to original authors' names, affiliations, and journal of publication. Reviews were recorded on a standard case report form and entered into a database for analysis. Discrepancies between reviewers were arbitrated by group consensus. Reviewers first made a final check of inclusion and exclusion criteria to exclude further any nonapplicable articles. Reviewers recorded the study setting, objectives, methods, results, and any additional comments.

Each article was assessed for the type of evaluation and categorized (Table 1). Two factors were considered in determining the type of evaluation: the presence of two or more alternatives, and the consideration of both input (costs) and outcomes. Evaluations that included two or more alternatives (i.e., concurrent control group, historical control, preintervention and postintervention design) were considered true analyses, whereas those that did not include a comparison were labeled descriptions. A description of the type of analysis was assigned to the evaluation and included the options of cost or outcome description, cost or outcome analysis, cost and outcome description, and true clinical economic evaluation. Those articles considered true clinical economic evaluations were subcategorized by type, options including cost-minimization analysis, cost–benefit analysis, cost-effectiveness analysis, and cost–utility analysis.[6]

Descriptive statistics were used to profile and characterize the articles within each data field abstracted by the reviewers, including the type of clinical service performed, the site of the study or evaluation, and the type of analysis performed.

RESULTS

The results of the search and screen process used are illustrated in Fig. 1. A total of 575 articles were found through the original search. A preliminary review of the abstracts of these articles identified 444 that did not involve the justification of clinical pharmacy services, and these were deleted from the set. Seven articles were added from the files of the authors, and 46 were identified through the secondary search of the articles found. Thus, 184 articles were subjected to full review. During full review, an additional 80 articles were found that did not meet the inclusion criteria: 44 did not review a clinical

Table 1 Criteria for assessing type of analysis

		Were both cost and outcomes considered?	
		No	**Yes**
Were two or more alternatives considered?	No	Cost description or outcome description	Cost and outcome description
	Yes	Cost analysis or outcome analysis	True clinical economic analysis Subcategories Cost-minimization analysis Cost–benefit analysis Cost–effectiveness analysis Cost–utility analysis

(Adapted from Ref. [6].)

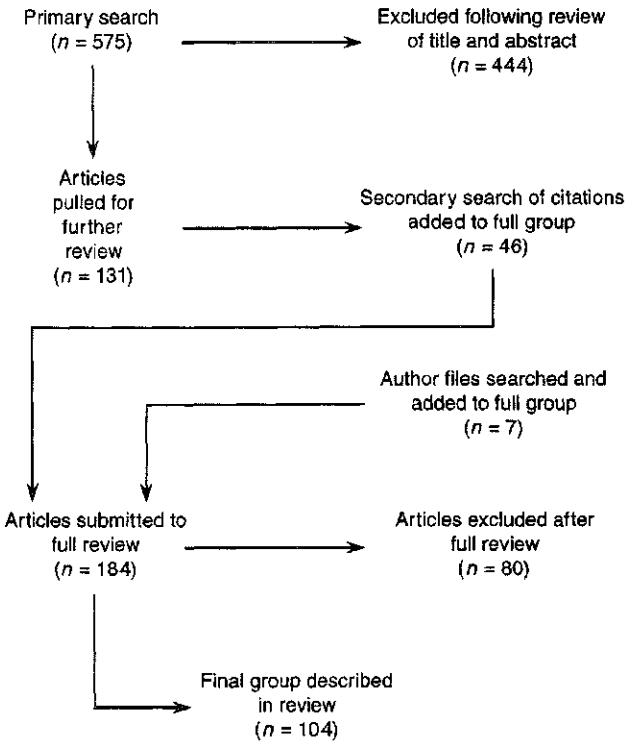

Fig. 1 Literature search method and results.

pharmacy service, 20 did not describe original work, and 16 failed on both points. An analysis of the final set of 104 articles is shown in Appendix 1.[7–110]

Articles are sorted in Appendix 1 by the type of clinical pharmacy service described in the evaluation. Four major categories were used in grouping articles by type of clinical pharmacy service: 1) disease state management, defined as clinical pharmacy services primarily directed at patients with a specific disease state or diagnosis; for example, a renal dosing program; 2) general pharmacotherapeutic monitoring, defined as clinical pharmacy services that encompass a broad range of activities based primarily on the needs of a geographically assigned group of patients; services provided may include patient drug regimen review, adverse drug reaction monitoring, drug interaction assessment, formulary compliance, or rounding with physicians; 3) pharmacokinetic monitoring services, defined as clinical pharmacy services that primarily involve evaluation of anticipated or actual serum drug concentrations and provision of subsequent dosing recommendations; and 4) targeted drug programs, defined as clinical pharmacy services that are primarily focused on a single drug or class of drugs and include predefined guidelines for provision of alternative therapy or dosing recommendations; for example, recommended switch from intravenous to oral administration of histamine$_2$-receptor antagonists (H_2RAs). Because of the number of articles describing targeted drug programs, those articles are further subcategorized in Appendix 1 based on the class of drug involved.

Provided in Appendix 1 are the following data for each article: 1) reference number; 2) the setting in which the evaluation was conducted; 3) a summary of the primary intent or objective; 4) a description of the analytical method of the evaluation; 5) number and type of alternatives included in the evaluation; 6) input cost components included in the evaluation; 7) outcomes evaluated; 8) a summary of the main results of the evaluation; and 9) miscellaneous comments about the evaluation made by the reviewer.

Articles from pharmacy-based journals dominated the set of articles. The most common journal source was the *American Journal of Health-System Pharmacy* ($n = 32$, 30%). *DICP/Annals of Pharmacotherapy*, *Hospital Pharmacy*, and *Hospital Formulary* were also common ($n = 19$, $n = 15$, and $n = 7$, respectively). Several foreign journals also provided articles.

The most common type of pharmacy service was targeted drug programs ($n = 49$, 47%). The specific drug classes described in targeted drug programs were most likely to be antimicrobials ($n = 27$) or H_2RAs ($n = 17$). Articles classified as general pharmacotherapeutic monitoring made up 36% ($n = 38$), pharmacokinetic monitoring services 13% ($n = 13$), and disease state management 4% ($n = 4$).

Table 2 summarizes the settings of the studies included in this evaluation. The settings of most studies were university or community hospitals ($n = 33$ and $n = 25$, respectively). University-affiliated community hospitals and government hospitals were also common ($n = 12$ and $n = 10$, respectively). Less common settings were ambu-

Table 2 Settings of cost-justification studies

Setting	Number of studies
University hospital	33
Community hospital	25
University-affiliated teaching community hospital	12
Government hospital	10
University-affiliated ambulatory clinic	8
Government-affiliated ambulatory clinic	5
Health maintenance organization clinic	4
Multicenter, multisite	3
Community pharmacy	2
University-affiliated government hospital	2

Table 3 Analytic methods of cost-justification studies[a]

Method	Number of studies
Outcome analysis	37
Outcome description	33
Economic analysis	19
Cost and outcome description	13
Cost analysis	1
Cost description	1

[a]Refer to Table 1 for classification analysis.

latory clinics of various affiliations, health maintenance organizations, and community pharmacies.

Table 3 summarizes the analytic methods used in the included articles. Although 19 (18%) articles were considered full economic analyses (by definition, considering two or more alternatives and measurement of both input costs and outcomes), most were less rigorous. The most common types of studies were outcome analyses ($n = 37$, 35%), which considered two or more alternatives but excluded consideration of the costs of providing the service, and outcome descriptions ($n = 33$, 32%), which failed to consider two or more alternatives and did not consider the cost of providing the service.

The study design of the included articles was further analyzed by individually considering the use of a comparison group (alternative) and by the types of input costs and outcomes measured. Sixty-one (59%) studies included a comparison group, whereas 43 (41%) did not and were therefore considered to be descriptive. The study designs used in papers that had a comparison group were a concurrent control group ($n = 21$), a historical control group ($n = 10$), and preintervention and postintervention groups ($n = 30$). Precontrols and postcontrols were differentiated from historical control designs in the temporal relationship to the intervention. If a study compared measurements taken immediately prior to an intervention and immediately after, it was coded as a pre/post design. If a longer period of time elapsed between comparison groups (e.g., comparing data from the study period to the same month 1 year earlier), it was defined as a historical control.

Seventy-one studies (68%) did not evaluate the cost of providing the clinical service as part of the economic evaluation of that service. Most commonly, costs were considered as an outcome or consequence of the service (i.e., as in drug costs avoided) rather than as an input (i.e., as in the investment required to establish and maintain the program under study). Of the 33 (32%) studies that did consider some input costs, the most common cost assessed was personnel ($n = 25$). In these cases, the costs of the program under study were quantified in terms of salary and/or benefits associated with providing the program or service. Some studies used charges (i.e., hospital room, emergency room) rather than true costs.

Outcomes or consequences of the services described were considered in all the articles. The most common ($n = 80$, 77%) outcome measured was drug costs avoided (i.e., the impact of the program on reducing use or cost of a particular drug). Other nonfinancial outcomes were also measured, including length of hospital stay ($n = 14$, 13%), use of nonpharmaceutical resources, rates of adverse drug reactions, frequency of pharmacist-driven therapeutic interventions, and qualitative changes in prescribing patterns. True clinical patient outcomes were considered in few studies.

Ninety-three (89%) of the articles described beneficial financial impact of the clinical pharmacy service described. Many provided either gross cost savings or, in those that did consider input costs, net savings. Of the 33 studies that considered input costs, 31 (94%) demonstrated positive findings. Results of these were presented a number of different ways (Table 4).

Commonly these articles expressed net savings on an annual basis or for the time period of the study. For example, a study in 1992 described annual net cost savings of $221,056 for clinical pharmacy services provided in an ambulatory care clinic.[25] It did not, however, include a control group. In other cases, savings were expressed per patient admission or per patient-day. In 1993, a well-conducted and controlled evaluation described an average net savings of $377 per patient admission as a result of clinical pharmacists assigned to selected inpatient medical services.[14]

In seven articles, results were expressed as benefit:cost ratios. They differed in type of clinical pharmacy service, site of provision of service, and resources invested in the service (Table 5). Nevertheless, the results were impress-

Table 4 Studies that considered input costs of providing service

Method of expressing results	References[a]
Net savings annualized or for time period of study	[8,9,11,18,20,24,25,31,36, 45,51,53,55,68,79,82,91, 94,98,104,110]
Net savings/patient-day or patient admission	[13–15,20,38,52,60,71]
Benefit : cost ratio	[11,14,15,41,51,60,98],
Other	[10,29]

[a]References may be listed more than once if results were expressed in different formats.

Table 5 Studies allowing calculation of benefit:cost ratio

Setting	Clinical service	Objective	Benefit:cost ratio
University hospital[11]	Pharmacotherapeutic monitoring	To examine cost benefit of clinical pharmacy intervention and documentation system	1.98:1
Government hospital[14]	Pharmacotherapeutic monitoring	To study effect of clinical RPh on health care outcomes	6.03:1
HMO clinic[15]	Pharmacotherapeutic monitoring	To measure impact of pharmaceutical services on overall health care costs and to estimate RPh productivity	3.2:1
University hospital[41]	Pharmacotherapeutic monitoring	To evaluate impact of clinical pharmacy service on hospital costs using cost–benefit analysis	1.08:1 and 1.59:1
University-affiliated[51] community hospital	Pharmacokinetic monitoring	To determine cost benefit of pharmacokinetic services for patients receiving aminoglycosides	75.84:1 and 52.25:1
University hospital[60]	Pharmacokinetic monitoring	To evaluate impact of computer-assisted aminoglycoside dosing	4.09:1
HMO clinic[98]	Target drug program	To evaluate impact of clinical RPh intervention program on cost of H_2RA therapy	4.3:1

HMO, health maintenance organization; H_2RA, histamine$_2$-receptor antagonist.

ively positive, with calculated benefits to cost ranging from 1.08 : 1 to 75.84 : 1 (mean 16.70 : 1).

DISCUSSION

Assessment of the Literature

The conclusions drawn from our review and evaluation of literature assessing the economic value of clinical pharmacy services published from 1988–1995 are multifocal. The total number of articles published on this topic has grown, as demonstrated by the number in this review (104, average 13/yr) versus the original prospectus (58, average 4/yr), which included articles published from 1974–1987. Although the number of published articles on this topic appears sufficient, an opportunity does exist for improvement in the quality of study design.

A large percentage (41%) of the articles we reviewed did not include a comparison group. They did not incorporate a study design that would allow one to control variance, which therefore makes it difficult for the reader to confirm the validity or extrapolate the results to other practice settings. This is not to say that these articles are without value, however. Many are excellent descriptive reports that provide insight and experience from which others may learn.

Sixty-eight percent of studies did not consider the costs associated with providing clinical pharmacy services as a factor in the economic evaluation or justification of that service, thus making it difficult to demonstrate true economic justification of the service. For those studies that did consider some input costs, personnel costs were often singularly included, with nonlabor costs (i.e., overhead) being omitted. Furthermore, when charges were used, they were often misinterpreted as costs.

The outcomes measured tended to focus on financial consequences and not to include clinical or patient consequences. Without consideration of clinical outcomes, or without being able to make an assumption that clinical outcomes are unchanged, the true economic impact of the services studied could not be proved.

Despite the limitations of many of the articles as true economic evaluations, this literature contains a wealth of information pertinent to the clinical practice of pharmacy that serves to document innovative and successful experiences and programs. Of importance, we did find that when studies were well conducted (considered true economic evaluations), the results were likely to be favorable; that is, the studies were able to demonstrate net savings or positive benefit : cost ratios. Because of lack of standardization in reporting of results and variability in study design, it is difficult to make a general statement as to the degree of benefit derived from clinical pharmacy services. However, we were able to abstract calculated benefit : cost ratios from the seven applicable studies and describe a range of value from 1.08:1 to 75.84:1 (mean 16.70:1). In other words, for every

dollar invested in clinical services, on average $16.70 was saved.

These seven studies were conducted in a variety of practice environments—university hospitals (3), university-affiliated community hospital (1), governmental hospital (1), and health maintenance organization clinics (2). They evaluated a spectrum of pharmacist-delivered services including pharmacotherapeutic monitoring (4), pharmacokinetic monitoring (2), and targeted drug programs (1). Both of these considerations speak to what we believe to be the broad applicability of the studies' results.

Limitations

We undertook this review and evaluation with the intent of providing the reader a resource to access original literature published assessing the economic value of clinical pharmacy services, and to evaluate the quality of that literature. The articles included in this review represent only those published in standard literature. We did not consider unpublished studies and therefore our results may be subject to inherent publication bias (so-called "file drawer" effect). We included only articles that contained some consideration of the financial impact of clinical pharmacy services. Certainly, many useful articles describe and evaluate clinical pharmacy services, but focus on nonfinancial outcomes and impact, and are worthy of review. Finally, our review of the literature, although intended to be systematic and thorough, may not have captured all the published literature on this topic.

Recommendations

Having reviewed and evaluated the published literature on the economic value of clinical pharmacy services, we make the following recommendations to clinicians, investigators, authors, reviewers, and journal editors:

1. Future economic evaluations should incorporate sound methodology and study designs. Study designs should control for variance by using a comparison group such as a historical control, concurrent control, or pre- and postintervention measurement.
2. Consideration should be given to the input costs, that is, the costs of providing the service, as part of the economic evaluation. These costs should include direct and indirect costs if possible. Where charges are used, they should be appropriately labeled and interpreted as such.
3. Outcome measurements should include more than just drug costs avoided. Nonfinancial outcomes such as clinical patient outcomes are important and should be part of the evaluation of any service that affects patient care. Using a disease state management approach rather than the targeted drug approach to cost justification may help to identify important outcome measurements that should be considered.
4. The concept of opportunity costs (i.e., money spent on one resource that cannot be spent for other purposes) should be explored. The value of any given service should be weighed against the possible services that might be provided. The concept of opportunity costs becomes even more important as health care downsizing and restructuring occur.
5. Clinical pharmacy services provided in settings outside the traditional hospital should be included in future economic evaluations.

CONCLUSION

It is hoped that the data summarized in this article will assist individual pharmacists, departmental managers, and health system administrators to document and recognize the cost effectiveness of pharmacists' clinical services. Pharmacy practitioners should take pride in both the quantity and strength of this literature, and feel empowered to use it to justify further expansion or refinement of their caregiving responsibilities. Attention to our recommendations regarding the design and performance of future economic evaluations of clinical pharmacy services will further add to the strength of this literature and the conclusions that may be drawn from it.

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Appendix 1 Evaluations of economic value of clinical pharmacy services—1988–1995

Setting	Objective (as stated by authors)	Analytic method	Comparison group	Input costs	Outcomes included	Results measured	Comments
Disease state management							
CH[7]	To evaluate impact of benzodiazepine guidelines on cost and quality of care of patients hospitalized for alcohol withdrawal	OA	Control group	None	DCA, LOS	Mean drug cost decreased from $1008/day to $59/day/patient; mean ICU LOS decreased from 4.1 to 1.1 days	Input costs not considered
UH[8]	To evaluate impact of clinical RPh on cost savings and patient outcome in asthma clinic	CBA	Historical control	Cost of clinic visit offset other savings	Cost of emergency room visits for asthma exacerbation	Cost savings $30,693 and $68,393 between study period and each of two control periods; savings derived from reduction in ER visits	Drug costs not considered; economic value of clinical outcomes (beyond ER visits) not assessed; no ratio calculated
CH[9]	To evaluate impact of renal function monitoring program, focusing on appropriate dosages of renally eliminated agents	COD	None	Personnel costs	DCA	Cost savings $5040 noted, with program cost $2700 for labor	No control group; clinical outcomes not considered; measured only what the cost of therapy would have been without intervention
UACH[10]	To conduct time and motion analysis of PCA vs. i.m. analgesia and evaluate impact on cost and quality of pain control	CBA	Historical control	Costs of drug, RPh, and nursing labor	LOS, cost of ADRs, quality of analgesia	Quality of analgesia increased with PCA, but so did cost and time required	Evaluated both RPh and nursing time; did not provide ratio
General pharmacotherapeutic monitoring							
UH[11]	To examine cost benefit of clinical pharmacy intervention and documentation system	COD	None	Personnel costs	DCA, type of intervention	Cost savings of $1.98/$1 invested, with total annual savings $7100	Missing relevant costs and outcomes

(*Continued*)

Appendix 1 Evaluations of economic value of clinical pharmacy services—1988–1995 (*Continued*)

Setting	Objective (as stated by authors)	Analytic method	Comparison group	Input costs	Outcomes included	Results measured	Comments
CH[12]	To assess the quality and cost avoidance of RPh interventions using physician assessors	OD	None	None	DCA, LOS	Positive impact on patient care, estimated reduced LOS by 3.7 days	Physician reviewers estimated reduction in LOS resulting from interventions
UH[13]	To cost justify clinical pharmacy service on general surgery team	COD	None	Personnel costs	DCA, type of intervention, clinical impact of intervention	Positive impact on outcomes; net cost avoidance of $441.46/patient	Small sample
GH[14] (Army)	To study effect of clinical RPh on health care outcomes	CBA	Control group	Personnel costs	LOS, drug costs/ admission	Average net savings $377/patient admission; cost : benefit ratio 6.03 : 1	Control group included
HMOC[15]	To measure impact of pharmaceutical services on overall health care costs, and to estimate RPh productivity	COD	None	Personnel costs, direct costs, overhead	Percentage of problematic drugs, use of service, DCA	Average total cost savings $644/patient; cost : benefit ratio 3.2 : 1	
GH[16] (VA)	To evaluate clinical RPh recommendations on number and costs of drugs	OD	Control group	None	DCA	Decreased average monthly drug cost/patient	Input costs not considered
UACH[17]	To describe program and determine cost savings from clinical pharmacy services provided in rehabilitation clinic	OD	None	None	DCA	Reduced hospital drug costs by $2700 during 6-mo study	Input costs not considered
CH[18]	To evaluate clinical pharmacy services and determine cost savings and justification for additional pharmacy staff	COD	None	Personnel costs	DCA	Annual net savings $25,862	
CH[19]	To evaluate impact of a clinical coordinator on costs avoided by the institution from clinical clinical intervention program	OA	Pre/post	None	DCA, NOI	Average monthly net savings $3739 and $4644 before and after clinical coordinator	

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Appendix 1 Evaluations of economic value of clinical pharmacy services—1988–1995 (*Continued*)

Setting	Objective (as stated by authors)	Analytic method	Comparison group	Input costs	Outcomes included	Results measured	Comments
UH[20]	To describe interventions made by clinical RPh and evaluate cost savings and cost avoidance impact	COD	None	Personnel costs	DCA, NOI	Cost savings of $69.11/patient-day; annual net savings $300,079	
UH[21]	To compare cost and quality of decentralized vs. centralized pharmaceutical services	OA	Pre/post	None	LOS, total cost/admission	Decreased average total cost/admission by $1293; decreased average pharmacy cost/admission by $155 for decentralized	
CP[22]	To examine value of clinical pharmacy intervention program in a community pharmacy setting and determine economic value	OD	None	None	DCA, NOI	Cost avoided of $3.47/prescription processed	
UACH[23]	To describe program to develop clinical pharmacy staff and determine cost avoidance to hospital resulting from the service	OD	None	None	DCA	Average estimated cost avoidance $9306/mo over 5 yrs	Input costs not considered
UH[24]	To evaluate and document impact of clinical RPh on costs avoided at tertiary care teaching hospital	COD	None	Personnel costs	DCA	Net annualized cost avoidance $897,350	
UAAC[25]	To evaluate impact of clinical RPh on cost and quality of patient care in ambulatory care clinics	COD	None	Personnel costs	DCA	Net annualized cost avoidance $221,056	Emphasized need for documenting interventions
UH[26]	To evaluate impact of clinical RPh on medical team	OD	None	None	Interventions documented	27% of interventions prevented serious effects	Input costs not considered

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Appendix 1 Evaluations of economic value of clinical pharmacy services—1988–1995 (*Continued*)

Setting	Objective (as stated by authors)	Analytic method	Comparison group	Input costs	Outcomes included	Results measured	Comments
MC, CH, MHF, SNF[27]	To evaluate impact of reactive clinical pharmacy interventions on cost and quality of patient care	OD	None	None	Cost impact of interventions documented	2.9% of pharmacy interventions prevented potential medical harm; limited cost impact	Input costs not considered; physicians assessed RPh service, introducing potential bias
GH[28] (VA)	To evaluate daily data collection of decentralized clinical pharmacy services	OD	None	None	DCA	Total savings $126,504 due to 2506 interventions provided	Input costs not considered; clinical outcomes not considered; no comparative group used to assess cost and outcome difference
GAAC[29]	To evaluate impact of clinical RPh's interventions on physician prescribing and costs in an ambulatory clinic	CBA	Control group	Personnel costs	Cost avoidance due to reduced number of prescriptions	Cost avoidance $4.63 for intervention group vs. $1.10 in control group; savings in prescription filling labor noted; labor costs associated with program offset by DCA	Clinical outcomes not considered; no ratio presented
UAAC[30]	To evaluate impact of ambulatory clinical pharmacy program and to justify personnel for the program	OD	None	None	Cost avoidance in drug and laboratory use	$19,000 in cost reduction for interventions, 184 patients; documented clinical outcomes after interventions	Discussed cost of personnel required for program, but did not factor cost into analysis; no comparison group for analysis
GAAC[31] (VA)	To evaluate impact of clinical RPh on cost and quality of patient care	CBA	Pre/post	Costs associated with program and dispensing prescriptions generated in the clinic	DCA	Total cost decrease of $22,241 during study period	Charts assessed for quality based on the rate of suggestion implementation, but actual patient outcomes not assessed
UACH[32]	To evaluate cost impact of clinical RPh in intensive care unit	COD	None	Personnel costs	DCA	Cost savings $10,010 (Canadian) documented over 3-mo study period; cost:benefit ratio 4 : 1	No control group; measured only what the cost of therapy would have been without intervention

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Appendix 1 Evaluations of economic value of clinical pharmacy services—1988–1995 (*Continued*)

Setting	Objective (as stated by authors)	Analytic method	Comparison group	Input costs	Outcomes included	Results measured	Comments
UH[33]	To evaluate impact of pharmacy faculty providing clinical pharmacy interventions on drug costs and pharmacy department revenue	OD	None	None	DCA and service revenue generated	Impact of 278 interventions evaluated, demonstrating drug cost avoidance $1661, generation of $6000 in revenue from pharmacokinetic consultations	No control group; measured only what the cost of therapy would have been without intervention
GAAC[34] (VA)	To evaluate impact of clinical RPh on drug prescribing and cost savings	CBA	Control group	Personnel costs	DCA	Decreased total number of prescriptions and associated ADRs; total cost of prescriptions filled in study period $3872 less than during control period; total cost to administer program $2250	No ratio presented; mentioned but did not quantify value of prevented ADRs
CH[35]	To evaluate impact of documentation system for clinical pharmacy services	OD	None	None	DCA	Cost avoidance ranged $2341–$7762/quarter during study	Input costs not considered; no control group; clinical outcomes not considered
CH[36]	To evaluate cost impact of implementing clinical pharmacy services in intensive care unit	COD	None	Personnel costs	DCA	During 32 days, cost avoidance $1651, labor cost associated with program was $2599	No control group; clinical outcomes not considered; small sample size (number of pilot days assessed, and short period of time/day)
MC, UH[37]	To evaluate acceptance and cost savings resulting from 2-yr postbaccalaureate PharmD student interventions	OD	None	None	NOI, DCA, laboratory cost avoidance	Estimated annual drug savings $3891	Input costs not considered

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Appendix 1 Evaluations of economic value of clinical pharmacy services—1988–1995 (*Continued*)

Setting	Objective (as stated by authors)	Analytic method	Comparison group	Input costs	Outcomes included	Results measured	Comments
CH[38]	To determine cost savings of clinical pharmacy service in a community hospital	CD	None	Personnel costs	DCA	Savings of $1.49/patient/day for clinical pharmacy services	Brief description of daily documentation activity to demonstrate cost savings
CH[39]	To describe impact of general clinical pharmacy interventions on hospital costs	OD	None	None	Physician acceptance, NOI, DCA	Total savings $15,525.81	Input costs not considered
CH[40]	To evaluate impact of comprehensive clinical pharmacy services on hospital costs	OA	Pre/post	None	DCA	Net cost savings $34.10/RPh-day	Input costs not considered; clinical outcomes not considered
UH[41]	To evaluate impact of clinical pharmacy service on hospital costs using cost–benefit analysis	CBA	Historical control	Cost of providing service	DCA	Cost:benefit ratios 1.08 and 1.59 for 2 ward-based groups	Clinical outcomes not considered
CH[42]	To determine impact of clinical interventions on cost and quality of patient care	OD	None	None	Number of inappropriate laboratory tests, DCA	Annual drug cost avoidance of $26,580	
UH[43]	To evaluate impact of PharmD student interventions	OD	None	None	NOI, physician acceptance	Decreased drug costs by 50.7%	
UH[44]	To document interventions of clinical RPh in emergency department	OA	Pre/post	None	DCA	Description of clinical and cost-saving interventions	Input costs not considered; clinical outcomes not considered
UAAC[45]	To evaluate impact of clinical pharmacy interventions on cost and quality of patient care	COD	None	Personnel costs	Physician acceptance, DCA, various quality indicators	Annual extrapolated cost savings $19,076	Documented cost and quality using daily patient data collection forms
UAAC[46]	To determine impact of clinical RPh on cost savings to the hospital and quality of patient care	OA	Control group	None	NOI, DCA	RPhs saved $176,724 annually	Extrapolated savings from 2-wk pilot

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Appendix 1 Evaluations of economic value of clinical pharmacy services—1988–1995 (*Continued*)

Setting	Objective (as stated by authors)	Analytic method	Comparison group	Input costs	Outcomes included	Results measured	Comments
CP[47]	To evaluate cost savings to pharmacy from interventions of community RPh	OD	None	None	Assessment of value of RPh interventions, cost of medical care avoided	Value of avoided care was $122.98/intervention; $2.32 savings/prescription screened	
UAAC[48]	To evaluate impact of clinical RPh on cost and quality of patient care	OD	None	None	Physician acceptance, patient outcome indicators, DCA	205 interventions made during 6-mo study; 80.9% made to increase quality; 18.1% to increase quality and decrease cost	
Pharmacokinetic monitoring service							
CH[49]	To determine effect of TDM program on inappropriate sampling times	OD	None	None	Unnecessary samples, patient charges	Charge avoidance $500,000 annually	Input costs not considered; charges vs. costs
UH[50]	To evaluate impact of educational efforts on use of SDCs	OA	Pre/post	None	DCA, number of drug assays	Increased number of drug levels ordered; decrease of $599 in hospital costs	Increased rational ordering of serum drug concentrations
UACH[51]	To determine cost benefit of pharmacokinetic services for patients receiving aminoglycosides	CBA	Control group	Variable costs, personnel costs, fixed costs	LOS, clinical response	Decreased LOS; decreased duration of febrile period; benefit:cost ratio 75.84:1 and 52.25:1	
CH[52]	To determine physician acceptance and impact of clinical pharmacokinetic recommendations on cost and quality of patient care	CBA	Control group	Variable costs, personnel costs, fixed costs	Acceptance by physicians, LOS, DCA, clinical response	Decreased LOS; decreased febrile period; decreased direct costs; cost of service $85/patient	
CH[53]	To evaluate impact of clinical pharmacokinetic service on cost and quality of patient care	CBA	Control group	Variable costs, fixed costs	LOS, clinical response, patient charges	Decreased length of treatment; decreased LOS; annual cost savings $113,934	Used charges rather than costs
CH[54]	To evaluate costs associated with clinical pharmacokinetic dosing service	OA	Pre/post	None	LOS, DCA	Cost reduction $107,000 associated with decrease in LOS; reduction of $14,000 in drug costs associated with program	Mentioned but did not value cost of system

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Appendix 1 Evaluations of economic value of clinical pharmacy services—1988–1995 (*Continued*)

Setting	Objective (as stated by authors)	Analytic method	Comparison group	Input costs	Outcomes included	Results measured	Comments
UH[55]	To evaluate impact of clinical RPh on appropriate serum drug concentration ordering	CBA	Historical control	Personnel costs	Cost of laboratory testing avoided	Increased appropriateness of serum drug concentration determination; cost of $1000 with savings of $3000	Clinical outcomes not considered; no ratio presented
UH[56]	To evaluate impact of pediatric pharmacokinetic service using guidelines as basis for appropriate monitoring	CA	Control group	None	Costs avoided through decrease in inappropriate monitoring	Annual cost avoidance $12,325 based on fewer inappropriate laboratory assays	Input costs not considered
CH[57]	To evaluate effectiveness of serum digoxin concentration monitoring, and determine cost impact of service	OD	None	None	NOI, timing of digoxin serum concentrations, laboratory costs avoided	Decreased number of digoxin serum drug concentrations ordered	Input costs not considered
UH[58]	To analyze need for therapeutic drug monitoring program for phenytoin	OA	Control group	None	Number and cost of drug assays, LOS and readmission rate	Overall cost savings after 1 yr of program $100.00	Charges vs. costs
UH[59]	To evaluate impact of therapeutic drug monitoring program for theophylline	OA	Control group	None	Number and cost of drug assays, LOS	Equal cost of RPh monitoring and savings after 1 yr	Charges vs. costs
UH[60]	To evaluate impact of computer-assisted aminoglycoside dosing	CBA	Control group	Service cost	LOS, room charge, DCA	$1311 savings/ patient in study group; CBA ratio of 4.09 : 1 in favor of study group	Used charges rather than costs
CH[61]	To compare RPh vs. physician dosing of aminophylline	OA	Control group	None	LOS, room charges, cost of concomitant drugs	Decreased LOS of 1.96 days; $490 savings/ patient in study groups	Used charges rather than costs
Target drug programs: Antiemetic agents							
UH[62]	To evaluate impact of prescribing guidelines for use of ondansetron on drug costs	OA	Pre/Post	None	DCA	15% reduction in amount of ondansetron dispensed from period before guideline implementation	Input costs not considered; clinical outcomes not considered

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Appendix 1 Evaluations of economic value of clinical pharmacy services—1988–1995 (*Continued*)

Setting	Objective (as stated by authors)	Analytic method	Comparison group	Input costs	Outcomes included	Results measured	Comments
Target drug programs: Antihypertensives							
HMOC[63]	To evaluate impact of clinical RPh consultation on cost of antihypertensive therapy in HMO family practice clinic	OA	Control group	None	Average daily drug costs	Decreased drug costs of $20.61/ patient-year	Input costs not considered
Target drug programs: Antimicrobials							
UAAC[64]	To assess impact of fluconazole guidelines and concurrent RPh intervention	OA	Historical control	None	Appropriate use, ADRs, DCA	Annual cost avoidance $65,520	Input costs not considered
UACH[65]	To describe experience with program for modifying dosing regimens of mezlocillin	OD	None	None	DCA	Annual cost savings $33,000 or $49.47/patient	Input costs not considered
UH[66]	To document cost containment of RPh antibiotic streamlining program	OD	None	None	DCA	Annual cost savings $47,700	Input costs not considered
UH[67]	To evaluate educational and intervention program promoting use of metronidazole for antibiotic-associated colitis	OD	Historical control	None	DCA	Estimated annual savings $38,829 based on decreased drug costs	Input costs not considered; clinical outcomes not considered
CH[68]	To evaluate impact of therapeutic intervention to alter metronidazole dosing	COD	Pre/post	Personnel costs	DCA	Annual savings $28,000	Input costs not considered
GH[69] (VA)	To describe antibiotic monitoring program and determine costs avoided to hospital from rational antibiotic use	OD	None	None	DCA, appropriateness	Total cost avoidance $42,512 during study period	Input costs not considered
UH[70]	To evaluate impact of target drug monitoring program for clindamycin on hospital costs	OA	Historical control	None	DCA	Cost avoidance $16,000 annually	Input costs not considered

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Appendix 1 Evaluations of economic value of clinical pharmacy services—1988–1995 (*Continued*)

Setting	Objective (as stated by authors)	Analytic method	Comparison group	Input costs	Outcomes included	Results measured	Comments
GH[71] (VA)	To evaluate impact of clinical RPh monitoring on i.v. ceftriaxone use (conversion to oral cefpodoxime)	CBA	Control group	Cost of treatment	Cost of treatment outcome	Cost savings $46.05/patient achieved, 1-day decrease in LOS	Input costs not considered; small sample
UH[72]	To evaluate antimicrobial management program and evaluate impact on cost and quality of patient care	OA	Historical control	None	DCA	Gross savings in antibiotic acquisition cost $483,032/yr	Cost associated with service considered, but not quantified
GH[73]	To evaluate cost impact of two DUE activities performed by undergraduate pharmacy students	OD	Historical control	None	DCA	Cefazolin dosing modification (q6h to q8h) resulted in savings of $18,000; substitution of metronidazole for clindamycin saved $21,000	Input costs not considered; clinical outcomes not considered
UH[74]	To evaluate cost impact of pharmacy-based antibiotic optimization program	OA	Pre/post	None	DCA	Savings of $12,640 realized after program implementation	Input costs not considered; clinical outcomes not considered
GH[75] (State)	To evaluate impact of RPh participating in patient care rounds on costs associated with antimicrobial drug use	OA	Pre/post	None	DCA	Cost reduction of $29,800 greater in study period vs. prestudy period	Input costs not considered
UACH[76]	To evaluate impact of clinical RPh-based antibiotic management program	OA	Control group	None	Drug and ancillary cost avoidance	Estimated cost savings $40,000 associated with drug cost avoidance and appropriate use of laboratory data	Input costs not considered; clinical outcomes not considered
UACH[77]	To evaluate impact of renal function monitoring program, focusing on appropriate dosages of imipenem	OD	None	None	DCA	Potential to save $11,500 annually by adjusting imipenem dosages on basis of renal function	Input costs not considered; no control group; clinical outcomes not considered

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Appendix 1 Evaluations of economic value of clinical pharmacy services—1988–1995 (*Continued*)

Setting	Objective (as stated by authors)	Analytical method	Comparison group	Input costs	Outcomes included	Results measured	Comments
UACH[78]	To evaluate cost impact of computerized antibiotic monitoring program	OA	Historical control	None	DCA	Predicted cost avoidance approximately $80,000 in control vs. study periods, but actual cost reduction attributed to program >$200,000	Cost associated with providing program mentioned but not quantified
UH[79]	To evaluate impact on hospital costs of antibiotic program using education and antimicrobial restriction	CBA	Pre/post	Costs of drug, labor, and program monitoring and implementation	LOS, infection frequency	Cost savings $14,250 annually with quality of care remaining constant	No ratio presented
MC, UH[80]	To conduct retrospective DUE to determine potential cost savings of ceftazidime dosage adjustment	OD	None	None	DCA	Ceftazidime dosing in elderly found to be in excess of labeled dosing because renal function not considered	Input costs not considered; clinical outcomes not considered
UH[81]	To evaluate impact of clinical RPh's intervention on antibiotic costs	OA	Pre/post	None	LOS, DCA	Audit results 3 mo before and after intervention revealed $3498.40 reduction in drug costs	
UH[82]	To determine impact of antibiotic monitoring program	CBA	Pre/post	Cost of printing intervention form	DCA	Net savings $17,000 annually	Clinical outcomes not considered; personnel costs not considered; no ratio presented
UAGH[83]	To evaluate impact of compliance with guidelines for third-generation cephalosporins	OA	Pre/post	None	Clinical and microbiologic indicators; DCA	Documented reduction of $27,000 over 6 mo in pharmacy expenditure for antibiotics	Input costs not considered
UACH[84]	To evaluate impact of antimicrobial intervention program	OD	None	None	Clinical and microbiologic indicators, laboratory costs, DCA	Savings $38,920 over 7 mo; projected annual savings $107,000	Input costs not considered; assumed quality and clinical outcome to be equal

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Appendix 1 Evaluations of economic value of clinical pharmacy services—1988–1995 (*Continued*)

Setting	Objective (as stated by authors)	Analytical method	Comparison group	Input costs	Outcomes included	Results measured	Comments
GH[85] (VA)	To evaluate impact of antibiotic policy on hospital costs and quality of patient care	OA	Pre/post	None	DCA, duration of antibiotics, LOS, mortality	Decreased monthly antibiotic costs by $7600; average savings $91,200 annually; fewer deaths; decreased LOS	
CH[86]	To describe cost savings to hospital resulting from clinical RPh and nursing antibiotic prescribing interventions	OD	None	None	DCA, NOI	Cost avoidance $23,993 during study period	Input costs not considered
UH[87]	To describe and evaluate dosing intervention program for imipenem	OA	Pre/post	None	ADRs, DCA	Decreased number of seizure episodes; cost savings due to dosage change	Retrospective chart review
GH[88] (VA)	To evaluate impact of concurrent antibiotic use program	OA	Pre/post	None	Length of antibiotic therapy, mortality, DCA, pharmacy cost, nursing cost	Decreased number of antibiotic doses/patient by 24%; 32% reduction in drug costs	Input costs not considered
UH[89]	To conduct DUE of prophylactic antibiotic therapy and determine cost savings to hospital	OA	Pre/post	None	DCA, number of inappropriate orders	Projected annual cost savings $25,000	Input costs not considered
UACH[90]	To evaluate impact of antibiotic therapeutic interchange program	OA	Pre/post	None	Efficacy indicators, ADRs, DCA	Decreased cost of daily antibiotic therapy in study group	Input costs not considered
Target drug programs: Acid-reduction therapy							
CH[91]	To document inappropriate use of i.v. H_2RAs and calculate cost avoided with oral conversion	COD	None	Personnel costs, direct costs	DCA	Cost avoidance range $606–8668 annually	No control group
CH[92]	To describe and evaluate the development of renal dosing intervention strategy for intermittent i.v. H_2RAs	OA	Pre/post	None	DCA	Decreased hospital cost/patient treatment day by 33% equal to $8053/yr	

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Appendix 1 Evaluations of economic value of clinical pharmacy services—1988–1995 (*Continued*)

Setting	Objective (as stated by authors)	Analytical method	Comparison group	Input costs	Outcomes included	Results measured	Comments
CH[93]	To evaluate cost savings to hospital resulting from clinical RPh recommendations for dosing i.v. H_2RAs	OA	Pre/post	None	DCA	Treatment cost decreased by $1.27/day; annual savings $838	Input costs not considered; clinical outcomes not considered
GH[94] (VA)	To evaluate impact of educational intervention with guideline implementation	CBA	Pre/post	Personnel costs	DCA	Annual cost avoidance of $25,000 associated with decreased use of acid-reducing therapy; estimated cost of program $3000	Clinical outcomes not considered; no ratio presented
GAAC[95] (State)	To evaluate impact of concurrent DUE program on costs associated with acid-reducing therapy	OA	Pre/post	None	DCA; clinical outcomes including antacid use and ordering of gastro-intestinal tests	Cost avoidance of $327,273 attributed to program, with no significant increase in antacid use of number of upper gastrointestinal studies	Input costs not considered
UH[96]	To evaluate cost impact of program authorizing clinical RPh conversion of drugs from parenteral to oral route	OA	Control group	None	DCA	Cost avoidance $53,950 with decrease in length of parenteral therapy	Clinical outcomes not considered; mentioned but did not quantify labor cost associated with program; mentioned but did not calculate ratio
UAAC[97]	To evaluate impact of guideline-based intervention program on cost of H_2RA therapy	OD	None	None	DCA	Total cost avoidance $47,672 during first 6 mo	Input costs not considered; no control group; clinical outcomes not considered
HMOC[98]	To evaluate impact of clinical RPh intervention program on cost of H_2RA therapy	CBA	Pre/post	Personnel costs	DCA	Annual savings $14,600, with labor costs of $3400; calculated cost : benefit ratio 4.3 : 1	Clinical outcomes not considered; useful model for justification of program provided outcomes considered

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Appendix 1 Evaluations of economic value of clinical pharmacy services—1988–1995 (*Continued*)

Setting	Objective (as stated by authors)	Analytical method	Comparison group	Input costs	Outcomes included	Results measured	Comments
CH[99]	To evaluate cost impact of therapeutic interchange program for H_2RA therapy	OD	None	None	Drug and ancillary cost avoidance	Estimated cost avoidance $37,565/yr	Input costs not considered; no control group; clinical outcomes not considered; included sunk costs (nursing costs associated with additional doses of drug) as costs avoided
CH[100]	To evaluate impact of therapeutic interchange program for H_2RA therapy	OD	None	None	DCA	Total $145,557 in cost avoidance in first yr of program	Input costs not considered; no control group; clinical outcomes not considered
HMOC[101]	To evaluate cost impact of educational interventions in improving use of H_2RA therapy	OA	Pre/post	None	DCA	Study group had fewer prescriptions, less expensive prescriptions, and more appropriate prescriptions after educational interventions than control group	Input costs not considered; clinical outcomes not considered; small sample (number of prescribers involved in intervention)
UACH[102]	To describe impact of therapeutic interchange program for H_2RAs on cost and quality of patient care	OD	None	None	DCA, ADRs, assessment of treatment failure	Estimated annual cost savings $16,000; reduced parenteral H_2RA use	Retrospective analysis; no evidence of increased treatment failure or adverse patient outcome
UH[103]	To evaluate impact of ranitidine i.v. to oral conversion project on cost savings to hospital	OD	None	None	DCA	Decreased number of days of i.v. acid-reducing agents; annual savings $23,425	
UH[104]	To evaluate impact of clinical RPh monitoring and intervention program on i.v. H_2RA therapy	CBA	Control group	Personnel costs	Number of i.v. doses and days of i.v. drug, DCA	Lower mean number of inappropriate doses in study group; projected net annual savings $15,766.37	No ratio presented

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Appendix 1 Evaluations of economic value of clinical pharmacy services—1988–1995 (*Continued*)

Setting	Objective (as stated by authors)	Analytical method	Comparison group	Input costs	Outcomes included	Results measured	Comments
UH[105]	To conduct prospective cost analysis of educational efforts to change inappropriate prescribing of H_2RAs	OA	Pre/post	None	Physician prescribing pattern, DCA, number of drug interactions	Savings of $250,000 estimated for 1st yr of program	Input costs not considered
UAGH[106]	To evaluate impact of i.v. to oral switch program for ranitidine	OA	Pre/post	None	DCA, pharmacy preparation costs	Cost avoidance $4214	Input costs not considered
UH[107]	To evaluate impact of H_2RA program on cost and quality of patient care	OA	Pre/post	None	Patient outcome, ADRs, drug interactions, DCA	Decreased cost but preserved quality	Input costs not considered
Target drug programs: NSAIDs							
GAAC[108] (VA)	To evaluate impact of clinical RPh activities in an ambulatory clinic	OA	Control group	None	DCA	Greater reduction in NSAID use in clinic staffed by RPh, resulted in cost savings of $38,776 more than control group	Input costs not considered; clinical outcomes not considered; data collected in 1985–1986, report not published until 1991
CH[109]	To describe target DUE program and determine impact on drug and labor costs	OA	Pre/post	None	DCA, NOI	Net annual savings $18,756	Considered personnel costs
UAAC[110]	To evaluate effect of pharmacist-managed anticoagulation clinical on therapeutic outcomes and costs	CMA	Control group	Charge for service	Hemorrhagic events, thromboembolic events, frequency and charge for clinic visits, ER visits, hospital admissions	Improved clinical outcomes, charge avoidance $4073/person-year	Included clinical outcomes, used charges rather than costs

CA, cost analysis; CBA, cost–benefit analysis; CD, cost description; COD, cost/outcome description; CMA, cost-minimization analysis; OA, outcome analysis; OD, outcome description; CH, community hospital; CP, community pharmacy; ER, emergency room; GAAC, government-affiliated ambulatory clinic; GH, government hospital; HMOC, health maintenance organization clinic; MC, multicenter; MHF, mental health facility; SNF, skilled nursing facility; UAAC, university-affiliated ambulatory clinic; UACH, university-affiliated community hospital; UAGH, university-affiliated government hospital; UH, university hospital; DCA, drug costs avoided; DUE, drug use evaluation; NOI, number of interventions or recommendations; ADRs, adverse drug reactions; H_2RA, histamine$_2$-receptor antagonist; ICU, intensive care unit; LOS, length of hospital stay; NSAIDs, nonsteroidal anti-inflammatory drugs; RPh, pharmacist; SDC, serum drug concentration; TDM, therapeutic drug monitoring.

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Electronic Prescribing

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INTRODUCTION

More than 17,000 brand and generic names for medications are currently approved for prescribing in North America.[1] Of those 17,000 chemical entities, a surprising amount have similar dosages. Furthermore, many names of the medications prescribed today are spelled or pronounced in similar ways. This can lead to a substantial number of errors due to the misinterpretation and/or misuse of abbreviations, chemical names, and dosages.[2] A study by Lesar et al. evaluated 696 clinically important errors in a 631-bed tertiary hospital and found that errors of nomenclature (incorrect drug name, dosage form or abbreviation) accounted for 13.4% of all medication errors. The authors further found that one in six errors involved the miscalculation of dosages, incorrect placement of a decimal, incorrect unit of measure, or an incorrect administration rate.[3] Although poor transcription of a medication order is an obvious contributing factor for these types of errors, other factors at the point of prescribing also play a role. Lesar et al. found that the most common types of errors made were due to the inappropriate application of drug therapy knowledge (30%) and the inappropriate use of knowledge regarding patient factors related to drug therapy (29.2%).[3]

Physician order entry has been recommended as one possible solution to help to prevent these types of medication errors.[1] Initially, the goal of prescribing automation was to decrease the potential for error due to the misinterpretation of handwritten orders. However, the capabilities of computers used to aid in medication order entry now exceed common word-processing duties. Newer systems have allowed clinicians to link patient data to the prescribing process. Clinicians can use these data to ensure that the drug dose, timing, and dosage form are correct, while checking for drug interactions, duplicate therapy, allergies, or disease-state contraindications. A study by Bates et al. found a greater than 50% reduction (10.7–4.86 events per 1000 patient days) in nonintercepted serious medication errors after a hospital-implemented direct physician order entry.[4] Another study found a significant reduction in errors due to allergies (76%) and excessive drug dosages (78.5%) after implementation of a computerized antiinfective management program.[5] Due to these and other study results, the National Patient Safety Partnership has recommended implementation of direct order entry strategies.[1]

DESCRIPTION OF ELECTRONIC PRESCRIBING

Direct order entry, or electronic prescribing, is not limited to the inpatient setting. Electronic prescribing encompasses all computer-driven automated processes used to write a prescription for a patient. Within the past few years, technological advances have allowed electronic prescribing to be performed in an ambulatory setting. This process is executed in many ways. Early versions of electronic prescribing devices consisted of a stand-alone computer terminal located at fixed points in physicians' offices.[6,7] These fixed terminals have expanded to use Internet web-based interfaces to access patient level information from a health plan, write prescriptions, and send prescriptions to a pharmacy to be filled.[8]

More recent advances in technology made possible by the personal digital assistant (PDA) have allowed physicians to electronically prescribe at the point of care. PDAs are handheld computers that typically run using a Windows- or other proprietary-based platforms. These PDAs use a touch-sensitive screen to maneuver through a menu-driven prescribing process that can execute a prescription in as little as three stylus taps.[9] The PDAs or other proprietary devices then upload the prescription via a network connection or modem to be printed, faxed, or electronically transmitted to a pharmacy.

INFORMATION AVAILABLE TO CLINICIANS

Electronic prescribing devices provide several sources of information to prescribers at the point of care provided to

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patients. Depending on the level of programming sophistication, and the database links built into the prescribing device, the clinician can access patient-specific formulary lists, manufacturer recalled medications, and a host of clinical references while choosing a therapy. The devices can also be used to review any managed care disease treatment protocols at the point of prescribing. It is also possible for the prescriber to perform drug utilization review (DUR) analyses to detect any possible drug–drug interactions, therapeutic duplications, drug–disease contraindications, drug allergies, past adverse reactions, and inappropriate dosing levels. These therapy edits are either provided real-time or as possible problems detected upon transmittal to the electronic prescribing vendor's server. Finally, electronic prescribing devices allow the user to provide informational leaflets to patients about their specific therapy.

PRESCRIPTION DESTINATION

Once the prescription has been entered, most electronic prescribing systems allow prescribers to transmit prescriptions directly to retail or mail order pharmacies electronically or by facsimile. However, some systems use an intermediary server to process prescriptions before sending them to a pharmacy. The limiting factor for electronic disposition of prescriptions is the ability to receive the data. Currently, a large percentage of pharmacies are not web enabled, and an even larger number of pharmacies do not operate on an electronic data interface that can speak to a prescriber's electronic prescribing devise. The solution rapidly being accepted to reconcile these inequities is a standard data transfer protocol called SCRIPT created by the National Council for Prescription Drug Programs. This standard (approved by the American National Standards Institute) has been accepted by most electronic prescribing device companies, and is rapidly being adopted by large chain drug stores.[10,11]

Who ultimately pays for the electronic prescribing capability is dependent on the electronic prescribing vendor. Some companies charge prescribers a basic monthly fee that ranges from $20–$250 per prescriber per month, depending on the level of information provided at the point of prescribing. This fee typically includes hardware, software, network connectivity devices, upgrades, and a local server.[9,10] Other companies provide hardware and software free of charge to prescribers and charge a second party for the use of the system. This second party is typically a pharmacy benefit manager or pharmacy, and the fees range from $.10–$.20 per prescription.[10]

ADVANTAGES OF ELECTRONIC PRESCRIBING

Electronic prescribing technology promises to bring many benefits to the current system of prescribing. The technology promises to bring greater efficiency to the prescribing process and reduces the likelihood of medication nomenclature errors. The following points highlight the potential benefits of adopting an automated prescribing system:

- Current, unbiased drug information and references can be provided real-time to clinicians, including educational updates for existing or new chemical entities and manufacture recalls of medications. This information could include recommended dosing, available routes of administration, and patient educational materials.[1,12]
- Patient-specific insurance information can be provided to prescribers at the point of care, including formulary lists and disease protocol information.[13]
- Patient-specific medical histories can be provided to prescribers at the point of care, including last filled medications, past adverse events, drug allergies, and medical conditions.[13]
- Pharmacies and physicians will need to spend less time contacting each other and insurance companies to overcome formulary restrictions and problems found upon drug utilization review, and to clarify illegible handwriting.[1,14]
- Physicians and pharmacists can expedite refill requests electronically rather than through person-to-person communication.[1]
- Computers can expedite data exchange between health care professionals who represent other parts of the patient's health care management team. The sharing of patient data could lead to less preventable adverse drug reactions and therapeutic duplications. The provision of diagnosis data along with prescription information also allows other heath care providers to check for therapy–diagnosis mismatches.[1,14]
- Computers can inform prescribers about lower-cost alternatives and generic availability at the time of prescribing.[1]

DISADVANTAGES OF ELECTRONIC PRESCRIBING

Conversely, electronic prescribing has a few potential disadvantages. Most of these disadvantages stem from the potential of the technology to be used for other purposes

apart from which it was intended. The following is a summary of potential misuses of the new technology:

- The potential exists for a patient's confidentiality to be violated. Some of the companies offering electronic prescription solutions download patient information to a vendor-based server for DUR checks. The security of this information and what it is used for beyond the prescribing process creates the potential to impinge upon the privacy of the patient's medical information.
- The receipt of a prescription can be subject to several market barriers. First, the pharmacy must have the electronic capability to receive the data. Second, the pharmacy must accept the patient's prescription drug plan and be willing to operate under the financial constraints imposed by the electronic prescribing provider. Finally, the potential exists for pharmacy benefit managers (PBMs) to use electronic prescribing technology to route prescriptions to preferred pharmacies such as mail order companies.
- Physicians will be prompted to adhere to formulary restrictions and PBM-driven disease protocols more frequently. As a result, evidence-based prescribing may become more dependent on the use of appropriate clinical knowledge by PBMs rather than health care providers.
- This technology can provide a false sense of security concerning the clinical judgment of the software programming. The programming is limited to the data it receives and the problems it is designed to detect. The innate ability of clinicians to question and rationalize is integral to the process of appropriate prescribing. However, electronic prescribing technology will make it easier to overlook the clinician's importance to the process.
- Theoretically, it is possible that electronic prescribing devices will allow unimpeded access to physicians by whoever is willing to pay for that access. Physician detailing may become more prevalent through these devices and could possibly be confused with unbiased medication information.

IMPACT ON PRACTICE OF PHARMACY

The advent of electronic prescribing will decrease pharmacists' roles in many areas. In dispensing roles, pharmacists will have less responsibility for order entry, PBM formulary management, and disease protocol adherence. Furthermore, a large number of DUR functions will be taken care of before the patient's order is received in the community or hospital pharmacy. However, the dispensing pharmacy may still function as a redundancy check on these issues, continuing to act as a patient advocate to manage the appropriateness of patients' drug therapy. The pharmacist will still operate as an integral check and balance concerning overlooked problems and missed patient information pertinent to a patient's effective drug treatment.

The functions performed by the electronic prescribing technology will most likely lessen the technical burden of the pharmacist, while augmenting the need for nontechnical clinical judgment. This augmentation of clinical judgment should manifest primarily in the review of a patient's situation and pharmacotherapy plan to identify barriers to the desired patient outcomes.[15] Although the more obvious problems will have a higher likelihood of being addressed at the point of prescribing, the pharmacist will still be needed to identify missed pharmaceutical errors related to dosage route, timing, duration, frequency, interaction, contraindication, and allergies. The main emphases of the pharmacist will likely shift to identifying and treating mismatched medications and indications, drug overuse and abuse, drug-induced problems, improper drug use, and potential medication errors.

With a decreased need for pharmacists to identify obvious problems associated with pharmaceutical therapy, the pharmacist should be free to concentrate on patient-centered therapy issues. Pharmacists can spend more time with patients identifying barriers that might prevent a patient reaching an optimal outcome. Pharmacists can then address these issues with education and proactive adjustments in the patient's therapy. The pharmacist can concentrate more time on educating patients to better monitor their therapy to increase the likelihood of maximal therapeutic benefit without troublesome misadventures. Furthermore, the pharmacist could concentrate on therapeutic outreach programs such as "brown bag" clinics, diabetic care clinics, and asthma screening.

In a hospital setting, pharmacists can shift their focus away from dispensing roles, and take a more proactive role at the point of care. Lieder reported that the implementation of physician electronic prescribing at Vanderbilt University Medical Center (VUMC) allowed pharmacists to have a greater role in the prescribing process. Pharmacists reported that clinical evaluations were easier with electronic records available at the touch of a key. Pharmacists felt free to pursue other areas of need such as cost-saving issues (e.g., intravenous to oral conversions of medications). The technology seemed to promote the presence of pharmacists on the floors to provide drug information to other health care professionals. The VUMC pharmacy actually maintained the electronic prescribing

system and provided educational enhancements directed at physicians as the need for interventions in therapeutic areas arose. Furthermore, the pharmacy planned to expand its services to include an inpatient anticoagulant management program.[116]

CONCLUSION

The future appears very bright for electronic prescribing. Certainly, the upfront costs for implementing programs, and the refinement of hardware and software specifics are important issues to resolve. However, the benefits of improved care, streamlined workflow, and more efficient use of clinicians' time are important enhancements that have continued to encourage expansion of these technologies. As wider audiences use these applications, continued research is needed to assess the use and refinements necessary to optimally apply these important systems.

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Ethical Issues in Clinical Pharmacy

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INTRODUCTION

The *Encyclopedia of Bioethics* defines "bioethics" as: "The systematic study of the moral-dimensions—including moral vision, decisions, conduct and policies—of the life sciences and healthcare, employing a variety of ethical methodologies in an interdisciplinary setting".[1] "Clinical ethics" is considered to be a subspecialty of bioethics and refers to the daily decision making of those who care for the patient.

CLINICAL ETHICS—THE PROFESSIONAL RELATIONSHIP BETWEEN THE HEALTH PROFESSIONAL AND PATIENT

As emphasized by Diego Gracia,[2] the professional relationship between the health professional and patient is a social one, although it seems that no one else is involved. When speaking of "third parties," one delimits within a generic concept of society, a more precise one. In the professional relationship between the health professional and patient, there are "three parties." The relationship is not lineal but rather triangular with three vertices: the *patient*, *the health professional* (physician, pharmacist, or nurse), and the *society* (social structures: health institutions, health insurance, etc.).

One might think that the health professional and the patient make, in accordance with the principles of nonmaleficence and autonomy, the decisions they find to be pertinent. The third parties put them into practice, as if these were means or instruments to reach an "end": the health professional–patient decision. But the "third parties" are structures with their own entity. So much so that they are guided by a third principle distinct from that of the health professionals nonmaleficence principle and that of the patient's autonomy. The principle of the third parties or that of the society is that of "justice." The principle of justice has embodied itself in a political tradition.

Changes in the healthcare model can generate ethical conflicts. If healthcare is made universal, it covers the entire population. Due to economic crises and scarce resources, it is not possible to meet all needs, just the basic ones or those that can be legally claimed. In any case, the system should guarantee equal access to and fair distribution of limited health resources.

ETHICAL THEORIES AND PRINCIPLES AS A FRAMEWORK FOR DECISION MAKING

Despite the fact that the new codes of pharmaceutical ethics[3,4] include the basic principles upon which bioethics is based (i.e., beneficence, autonomy, and justice), they are not complete enough to serve as a framework for making decisions in concrete situations where the basic principles come into conflict. In this case, an ethical foundation and a method are necessary.

The primary foundations are summed up in three theories: the theory of virtue, the deontological theory, and the consequentialist theory. (The reader is referred to other sources for more information.[1])

Bioethics, basing itself on the moral canon of the human being and on the necessity, as a rational being, to morally justify one's own acts, adopts the four ethical principles: *autonomy* and *beneficence* which pertain to the private sphere of the individual and *nonmaleficence* and *justice* which pertain to the public sphere.[5]

Decision-Making Procedures in Clinical Ethics

For several years, decision trees have been used in clinical ethics, although generally in a simplified form without carriyng out a detailed calculation of probabilities. One of the first to use this procedure was Baruch Brody, but the model was more widely accepted due to its simplicity was that of David C. Thomasma. Albert Jonsen developed a procedure based on the language of "cases" and "maxims." Sir David Ross, a great English ethicist at the beginning of the twentieth century, established the principalist method of the analysis of concrete cases. In this method, he establishes two moments in the moral judgment. First, that of the *prima facie* obligations and then

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that of *actual* obligation—that which is a true duty in a concrete circumstance. In other words, the *prima facie* obligations are objectives that can be canceled by other *prima facie* obligations of greater urgency. According to D. Gracia, their present application consists of:[6]

- The "a priori" moment: The *prima facie* principles of autonomy, beneficence, nonmaleficence, and justice.
- The "a posteriori" moment: Real and effective principles where the *prima facie* principles that are in conflict are arranged in order of importance, taking into account the concrete situation and the foreseen consequences. The hierarchy can vary according to each person's perception of a concrete situation. For this reason, it is best to keep in mind the greatest number of possible viewpoints in an attempt to enrich the analysis as much as possible before making a decision.

Such is the primary objective of the so-called "Institutional Committees of Ethics."

Professor Diego Gracia uses a procedure based on the analysis of the principles and consequences, like that suggested by David Ross, and applies it to clinical ethics.

Decision procedure in clinical ethics[6]

1. Analysis of clinical history by problems (biological, social).
2. Analysis of the clinical biological data and discussion of findings.
3. Identification of possible ethical problems—differentiate, count, and define all the ethical problems found in the clinical history.
4. Selection of the problem that causes a fundamental conflict of values.
5. Study of the possible courses of action.
6. Selection of the optimum possibility, that which saves the most values in conflict.
7. Decision on the course of action to be taken.
8. Analysis of the strong arguments against the decision, as well as the reasons for the decision (ability to defend it publicly).

ETHICAL PROBLEMS IN THE PHARMACIST'S CLINICAL PRACTICE

Relationship Between Physician, Pharmacist, and Patient

The pharmacist, as a health professional, can become immersed in various ethical problems. These are not unique to the pharmacist; many health professionals must deal with these same problems.[7] Such conflicts develop within the framework of the relationship between health professional and patient discussed earlier. For teaching purposes and because therapy with medication is used on almost all patients, this relationship triangle could be modified. It could be given a new dimension by converting it into a tetrahedron with the relationship physician–pharmacist–patient at the base and the society at the upper vertex (Fig. 1). Neither nursing nor the family is being excluded, as they are included with the physician and patient, respectively.

Professionals within the clinical relationship should work within a legal framework that defines the domain of each and respects the following patient rights:

- Confidentiality is the obligation of all health professionals to not reveal to others, without permission of the patient, information relative to the sick person or the illness, which goes along with the right to confidentiality of the patient. But this is a *prima facie* obligation, not an absolute one. Thus, when another person is in danger or the law calls for it, an exception should be made.
- Privacy, a patient right, dictates that no nonauthorized persons have access to their room, clinical history, or databases where pertinent information can be found.
- Revealing clinical, diagnostic, therapeutic, and prognostic information to the patient, as long as legislation does not say anything to the contrary, is in the domain of the treating physician. This fact does not mean that the pharmacist cannot give the patient information on the prescribed medication. But, for the benefit of the patient, it is best that this be done within the framework agreed upon for the collaboration between physician and pharmacist.

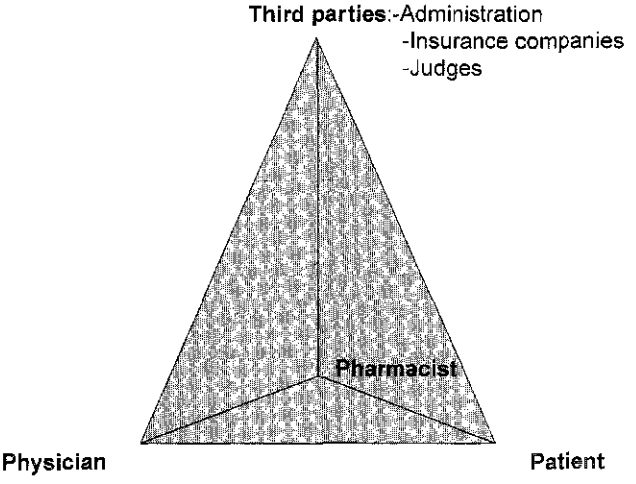

Fig. 1 Relationship between physician, pharmacist, and patient.

Definition of the Ethical Problem in Pharmacotherapy

T. L. Beauchamp and J. F. Childress define an ethical problem as a conflict between two moral obligations or norms. In general, there are two types of ethical problems:[8]

- Those originating from doubts about the morality of the act in itself in the face of strongly opposed arguments.
- Those originating from doubts about the decision whether to do one thing or another, both being mutually exclusive and implying a moral obligation.

The more specific problems in the pharmacist's clinical practice within this relationship are derivatives of the therapy with medication, nutrition, hydration, and placebo treatments.

We can define the ethical problem in pharmacotherapy as the conflict between moral obligations or norms that can put in danger the pharmacological treatment that is best for the patient.

Classification of Ethical Problems in Pharmacotherapy

The ethical problems in pharmacotherapy can be classified in the following manner.

Pharmacotherapeutic decisions

These are problems brought about by interprofessional differences (physician–pharmacist–nurse) in the making of pharmacotherapeutic decisions:

- In the evaluation of the benefits and risks of the necessary pharmacotherapy or that prescribed by a physician for a patient.
- In the inclusion of patient preferences in the pharmacotherapeutic decisions.

The analysis of these problems identifies a conflict of values or norms. On the one hand, in the first case it is the moral obligation of the pharmacist to promote the optimum treatment for the patient. In the second case, it is the obligation of the pharmacist to respect the autonomy and dignity of the patient.

The most adequate therapeutic decision is the selection of the therapeutic option that is most valid, taking into account the patient's circumstances in view of a highly probable diagnosis and prognosis, which is furthermore then accepted by the patient.

For this reason, as a precursor to the problem, it is assumed that the pharmacist will maintain professional competence, and that the pharmacist knows the clinical history of the patient as well as the circumstances of the case and preferably of the patient.

A conflict is generated when once the discrepancies have been discussed with the physician, it is socially expected that the pharmacist follow the medical order and dispense the medication prescribed.

This type of conflict can come about in the following circumstances:

- Omission of a validated and clearly suitable therapy.
- Prescription of nonvalidated therapies, which are considered to be neither suitable nor nonsuitable.
- Therapies that are clearly nonsuitable.
- The imposition of therapies on the patient on the part of the health professionals.
- Patient demand for a therapy not recommended by the physician.

Practical examples from scientific literature include obligatory sedation,[9] toxic analgesia,[10] the withdrawal of treatments (antibiotics, nutrition, hydration),[11,12] and the use of a placebo.[13]

Unavailability of medication

This is an ethical problem brought about due to lack of access to or unavailability of medication which is clearly suitable, with no equally efficient alternatives for a specific patient, orphan drugs, etc.

The present availability of scientific literature to all professionals in industrialized countries can lead to the knowledge of the existence of medications that are not commercially available in our countries. The professional could feel that it is more appropriate for the patient, but the administration does not approve its importation.

Another case would be when there is a lack of medicines in a given moment. This rationing would then imply the selection of a population to be treated, and it would be required that clear and fair criteria be used, such as the objective criteria of greatest benefit or due to prognostic factors or even by drawing lots.

The analysis of this problem introduces, on the one hand, the obligation of the pharmacist to promote the optimum treatment for the patient, and on the other hand, the obligation of the administration to establish explicit criteria for access to or availability of medicines being researched for severe illnesses or those which are life-threatening without satisfactory alternative treatments[8] (such as policies on orphan medicines, magistral formulation of nonregistered active ingredients, etc.).

A conflict can arise between the standard of evidence considered necessary by the administration, the randomized and controlled clinical study (RCT), and the desire of the patient to participate in an open trial, compassionated use (CU). This would mean a conflict between the principle of autonomy (patient) and that of beneficence (administration).

In favor of the open trials CU, it is argued that a minimum is being required (the RCT), which the patient does not want, and thus falls into a social paternalism. Furthermore, it is argued that the investigation of the clinical practice is possible, carrying out studies of results, without having to do studies with a control-arm or placebo.

In favor of RCTs, it is argued that since a vulnerable population is being dealt with, there could be a commercial exploitation upon introducing a medication in a pathology that does not have therapeutic alternatives, without having obtained a minimum standard of scientific evidence. If all of the patients with this pathology are offered this medication, no comparison can be made between this alternative and a placebo. Thus, there will be no certainty of its efficacy, and no other posterior therapy can be compared with a placebo.

Discrimination

This ethical problem is brought about due to a possible discrimination either in the use of or the cost for the patient of the pharmacotherapy.

Negative Discrimination in the Use of the Pharmacotherapy. This refers to the nonutilization of suitable therapies for elderly patients or women without situations of comorbidity which justify it.[14,15] The Committee of Ethical and Judicial Affairs of the American Medical Association has written reports about age-base rationing, gender, and black–white disparities in clinical decision making.[16]

In reality, negative descrimination does not produce any ethical conflict. It is not ethical in itself, as it does not respect the principles of nonmaleficence and justice.

Positive Discrimination in the Use of or in the Cost of the Pharmacotherapy. An example is the use of epoetin in patients who do not accept blood transfusions for religious and other reasons. The conflictive principles in this case could be beneficence and justice. Its use could be justified if justice is understood as equity, using the following argument: Blood transfusion is clearly against the beliefs of this group. These beliefs have been repeatedly infringed upon. According to the principle of equity, more should be given to the most needy, always applying explicit and transparent criteria.

As far as cost is concerned, positive discrimination occurs when the administration decides in favor of public financing of complete therapies for certain pathologies.[17]

Rationing

These ethical problems are brought about by the denial or restriction of medicines due to cost.

Rationing according to cost is the systematic and deliberate denial of some resources, although they could be very beneficial, because they are considered very expensive. Those cases for which there are less expensive alternative therapies, which are equally efficient and safe, are excluded. This would clearly be the most just (principles of rationality and distributive justice) and suitable therapy.

- Rationing of a clearly suitable therapy that does not have an alternative that is equally efficient and safe. The principles in conflict here would be those of nonmaleficence and justice. The rationing should be equitable and not infringe upon the "decent minimum." This is ethically acceptable when the rationing criteria are explicit and known to those potentially affected. This is understood within a framework of scarce resources in which all of the measures have been adopted for the rationalization of these.
- Rationing of therapies that are thought to be neither suitable nor nonsuitable (there is no proof for or against) which are restricted or denied due to their elevated cost. The conflict in this situation comes about between the principle of beneficence (if the physician orders the treatment) or the principle of autonomy (the patient wants the therapy) and that of justice. No conflict exists if the patient finances his/her own treatment, but it does exist if it is financed by the public health service. Generally, the principle of justice prevails over the other two, and all exceptions should be justifiable. For decisions for rationing to be just (distributive justice), they need to be adopted by the Health Administration.

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Ethical Issues Related to Clinical Pharmacy Research (ACCP)

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INTRODUCTION

Bioethics is a relatively new field of study concerning the investigation of ethical issues in medicine, health care, and the life sciences. From the standpoint of bioethics, clinical pharmacy research presents no novel ethical questions; however, the type and scope of issues involved differ from those faced by other practitioners. It is important for pharmacists to be aware of the ethical issues, give thoughtful consideration to them, and be sensitive to how they may affect their involvement in research. The current Code of Ethics for the practice of pharmacy virtually neglects issues encountered by pharmacists as they conduct clinical research.[1]

Pharmacists are expanding their responsibilities as health care practitioners by initiating and participating in clinical research.[2] These activities range from custodian of nonclinical and clinical trial information to principal investigator engaged in original research. For a discipline to survive as an entity, it must expand its body of knowledge continuously, rather than relying on other disciplines to create its knowledge base, including generating data that propose of confirm theories, principles, or relationships.

Because of the nature of ethics, this article presents more questions than it provides answers; it is difficult to predefine the right answers to ethical questions. Most experienced investigators will recognize the circumstances described and will have developed their own solutions. The article however, should prove useful to new investigators or trainees, perhaps as a mechanism to introduce discussion with mentors. It identifies ethical issues and questions in clinical pharmacy research regarding protection of human subjects, informed consent, conflicts of interest, clinical trial design, investigator independence, and scientific integrity.

HISTORICAL PERSPECTIVE

The Nuremberg Code[3,4] and the Declaration of Helsinki[5] are accepted international documents guiding the conduct of human clinical research (Appendices 1 and 2). The Nuremberg Code, established in 1948 after the war crimes trials of 1946, was the first internationally recognized code for human research. During the early 1950s, ethics committees for clinical research appeared in the United States. Until then, physician investigators and research institutes autonomously determined when investigations became dangerous and to what extent research subjects should be informed. Later the Department of Health, Education, and Welfare [the present Department of Health and Human Services (DHHS)], in response to reported abuses of the rights of individuals participating in certain federally supported research endeavors, mandated that all protocols be screened by institutional committees responsible for the protection of human subjects. The federal government committed itself when Congress established the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research in 1974. The commission issued the Belmont report in 1978;[6,7] with that, institutional review boards (IRBs) were born and principles of protecting the rights of human subjects participating in research began to evolve.

The Belmont report describes the basic ethical principles that underlie research involving human subjects: respect for persons, beneficence, and justice. The report discusses application of informed consent, assessment of risks and benefits, and selection of subjects. Its regulations require that IRBs have not fewer than five members who have the capability to judge research proposals in terms of community attitudes. Therefore, IRBs must include people whose primary concerns lie in the areas of legal, professional, and community acceptance rather than in the overall scientific design.

During the early 1980s, the DHHS developed and published rules and regulations for the protection of

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human research subjects' participation in federally funded research known as the Code of Federal Regulations. The Food and Drug Administration published similar regulations governing human research and investigations that are intended to support marketing permits for drugs, food additives, medical devices, biologic products, and electronic devices. These sets of regulations serve as the cornerstone for the oversight of safe human experimentation and guide all who participate in clinical research, (e.g., IRBs, investigators, research sponsors, research subjects). Generally, state agencies adopt the federal standards, and local research institutions interpret and apply them to all research activities involving humans.

PROTECTION OF HUMAN SUBJECTS

The IRB is charged, by federal, state, and local institutions with ensuring that principal investigators adequately protect the health and well-being of individuals whose participation may cause them to be at increased risk to hazards, defined broadly as physical, psychologic, sociologic, and legal. Thus, it is impossible to conduct clinical research in humans that would not affect one or more of these areas.

If local institutions receive any federal research money, all human research must be approved by the IRB. This is not the basis for IRB review but provides the incentive for local institutions to conduct studies that are ethical. The committee becomes involved in matters such as confidentiality, anonymity, and moral issues related to experimental activities. Approval from an IRB, however, does not relieve the principal investigator from the basic responsibility of safeguarding the health and welfare of participating individuals. This is a moral and professional responsibility that cannot be delegated.

INFORMED CONSENT

Informed consent comprises two distinct concepts. *Informed* means that the researcher provides something (information, assistance with a decision) to the subject. *Consent* means that there is something (permission) that the researcher requests from the subject. Consent must be given freely.

The informed consent process answers the moral question, when is it permissible to include competent people as research subjects? The answer is, if, and only if, they have given their free and informed consent. Inherent in this statement is the idea that investigators should ask for or request consent, not simply to get or obtain it. The mere existence of a signed form does not guarantee that the informed consent process worked for the benefit of the subject, but it can facilitate the process. The rights of the subject must be protected, and informed consent must be requested and obtained.

A risk–benefit assessment must be performed before a proposed investigation is submitted to the IRB. Because the true risk-to-benefit ratio generally is unknown, clear evidence for a favorable outcome must exist. Benefits may be gained by individual participants or by society as a consequence of the proposed activity.

Potential participants must agree in writing to the conditions of the study after receiving a complete and understandable explanation of the conditions of participation, the purpose of the activity, and the possible hazards involved. They must have the right to ask questions and to withdraw their consent at any stage of the activity.

Ethical Questions Concerning Informed Consent

Informed consent assumes that accurate information is being given, that the subject comprehends the information, and that the subject volunteers to participate. Do investigators emphasize each aspect appropriately? For example, how does the investigator ensure that the subject comprehends? Examples of methods used are having the subject repeat back in her or his own words the information immediately, and repeat it at some future time while involved in the research; and using a witness to sign the consent form.

While preoccupied with the informed consent form, investigators may neglect using required and appropriate language. How do pharmacists ensure that eighth-grade language is used on the consent form, and is it ever verified? If non-English-speaking people are being requested to participate in research studies, the informed consent form should also be written and presented in a language they understand. Computer programs and English teachers may be used to facilitate this process. Thus, two informed consent forms would be prepared, one in English and one in the appropriate non-English language. Investigators should ensure that these issues are not neglected.

How much information is necessary for potential subjects to be informed? Should investigators tell the subjects how much money they are compensated per subject recruited? It is probably unnecessary for subjects to understand how clinical research is funded (e.g., overhead fees, fees for certain services), unless this information would influence any reasonable person to participate (or not to participate). The pharmacy profes-

sion and society as a whole determine what reasonable people usually do, and this is susceptible to change over time. Research subjects have a right to know what is known, including the views of the investigators specifically and the pharmacy and medical professions in general. At minimum, investigators should give subjects the information that the average reasonable person would want to know.

Finally, how informed could a subject be about a new chemical entity when the aim of the study is to gain information for the first time in humans? To balance the apparent lack of information, the investigator is responsible for carefully monitoring the subject during all stages of the investigation.

Payment to Study Volunteers

The informed consent process raises ethical questions. The informed consent form may state that volunteers will be paid for their services, yet when does the payment become simply an inducement? Payment to volunteers for participation in drug trials is common and usually can be subdivided into two types, reimbursement for expenses incurred incidentally and wage payments. Reimbursement might cover expenses such as transportation costs, costs incurred by participation (e.g., extra blood sampling, new drugs or devices being used), and lost work time. Wage payments involve remuneration for services provided in serving as a research subject. These payments could be based on a number of factors, such as time commitment required, nature, and number of procedures performed, or to facilitate recruitment in a timely fashion. Payment should not constitute an inducement.

When ill persons are offered money over and above expenses to enter a clinical trial of a new drug therapy, the possibility of coercion exists. The reasoning is that if the patient is poor, they might not be able to afford the therapy without entering the trial. Contrast this experience with renally impaired volunteers recruited for a pharmacokinetic study of an antibiotic. Renal failure is not the target of therapy. The subjects receive no therapeutic benefit from participating and are paid as volunteers.

The IRBs should review research funding for appropriateness and possible coercion, specifically as it applies to subject recruitment. If the amount of payment is so high as to induce any reasonable person to participate, regardless of the risk, it is obviously too high. It becomes difficult, however, to determine when coercion is present because the majority of cases are not this obvious. Investigators should be able to justify any payment to research subjects. Several factors should be considered in justifying payment, such as the intensity of the protocol, whether it is funded and by whom, and the degree of benefit to subjects other than monetary.

Influence of Drug Therapy

Little information exists about how a patient's drug therapy influences the informed consent process. For example, can a patient who has had several doses of intravenous morphine give consent to participate in an acute myocardial infarction protocol? Sedated patients may not understand adequately what they are being told; therefore, they cannot make up their minds freely. As another example, how informed can patients be who are experiencing blurred vision from atropine? Does drug exposure influence continued participation or future consent? If there are any doubts, a family member, guardian, or patient advocate should be involved in the informed consent process.

Adverse Effects

In the context of a clinical trial, informing the patient of possible side effects could influence the outcome of the study. However, subjects have the right to know what may be expected to occur during participation. They must be informed of all possible adverse effects consistent with the information in the package insert (if available) and the information known from other studies.

ETHICAL QUESTIONS CONCERNING MORAL PRINCIPLES

Pharmacists, like physicians, have to be aware of the sovereignty of the patient. Although the protection of human subjects is critical, there is little opposition to the protection of human rights. However, opposition to other critical issues does exist to various degrees.

Questions of Fairness

When should we encourage repeated volunteering? Could studying the same pool of patients have a negative impact on the care of others? In other words, volunteering over and over again may; 1) deny the benefit of that research to others; 2) make research subjects bear too great a burden themselves; and 3) result in data that cannot be general-

ized to the rest of the population. Careful examination of the purposes of each investigation must be made to ensure that repeated volunteering is beneficial to subjects or to the experimental purpose. Thus, mere expediency of enrolling subjects does not justify studying the same individuals routinely. In some instances, such as pharmacokinetic studies, repeated use of the same subjects may be acceptable.

Therapeutic research is intended to benefit those who are the subjects of that research. What are the proper criteria for inclusion and exclusion that would ensure that everyone has a fair chance of benefiting from participating within the scope of the hypothesis being tested? The principle of justice or fairness dictates that subjects be selected equitably, in other words, giving everyone an opportunity, and not concentrating on individuals with or without certain diseases, those located in close proximity to the service institution, or those of a particular gender. For example, patients with liver dysfunction commonly are excluded from research protocols, but in fact are frequently the ones who receive the study drugs. Consider also, investigations using predominantly individuals of one race or ethnic minority simply because of their availability. Should we encourage the investigation of drug disposition in these patients, especially as they relate to the problem being studied?

Thus, selection of subjects has the potential to be an ethical dilemma. The Belmont Commission's interpretation of the requirement of justice[6–8] is seen in the following statement:

> The selection of research subjects needs to be scrutinized in order to determine whether some classes (e.g., welfare patients, particular racial and ethnic minorities, or persons confined to institutions) are being systematically selected simply because of their easy availability, their compromised position, or their manipulability, rather than for reasons directly related to the problem being studied. Finally, whenever research supported by public funds leads to the development of therapeutic devices and procedures, justice demands both that these not provide advantages only to those who can afford them and that such research should not unduly involve persons from groups unlikely to be among the beneficiaries of subsequent applications of the research.

If there are known populations of people in whom drug disposition and effect differ, should we neglect enrolling them in clinical trials? Certainly it is expedient to develop protocols that control for factors that may be a source of variability. However, in doing this, investigators must not systematically neglect important segments of the population.

Research involving healthy volunteers rarely benefits the subjects directly, yet may be harmful to them. Should pharmacists then encourage the development and use of new technologies or methods (e.g., noninvasive) to reduce risks while maintaining the scientific integrity of projects?[9] A simple venipuncture exposes both the subject and the investigator to a degree of risk above that which occurs in daily life.[6–9] If the study drug possesses a saliva : plasma concentration of approximately 1, are we justified in obtaining plasma samples? If the study intent is to screen for substances present, investigators should use noninvasive methods when possible rather than those requiring venipuncture.

Conflicts of Interest

Conflicts of interest issues are morally relevant because they represent temptations to do wrong. Million-dollar budgets have ways of creating ethical dilemmas for investigators. A prevalent problem is the influence of commercial interests on independent drug research. Medicine has emphasized disclosure to minimize this problem, but disclosure does not guarantee elimination of ethical dilemmas.

The American College of Clinical Pharmacy offers recommendations to minimize conflicts of interest in the accompanying position statement "Pharmacists and the pharmaceutical industry: guidelines for ethical interactions." The statement addresses questions such as, when is it permissible to accept an honorarium from a sponsor for providing a research talk, contributing to a symposium, or arranging a research-oriented training session? It also discusses the type of research that is appropriate to be funded. For example, it is unethical to perform a phase IV study for the sole purpose of familiarizing practitioners with a drug so that they will prescribe or recommend it frequently in the future. Ultimately, the pharmacist has the responsibility to maintain objectivity through the unprejudiced and unbiased performance of research activities regardless of the potential for personal financial gain.

Another example of a potential conflict of interest is the use of finder's fees to help to identify research subjects. A finder's fee is a fee paid to individuals, usually nurses, physicians, and pharmacists, who assist in locating potential research subjects. It may not be wrong to offer such a fee, but it is probably wrong for investigators to demand it. It would be unethical to deny a patient the opportunity to benefit from a study simply because the investigator would not receive the money. In lieu of paying finder's fees directly, some institutions

provide credit to a bookstore account or payment to a special account whose funds can be used only for educational purposes.

Individual Versus Social Interest

When is it permissible to deny some benefits, or put some subjects at risk, for the sake of research and the benefits it promises? For example, when is it permissible to perform cost-containment research, and what type of peer review and informed consent is necessary?[10] This is particularly relevant for pharmacists because many are involved in this type of data collection and analysis. It is possible that some subjects may receive a lower standard of care than that to which they are accustomed. Thus, experimental strategies that reduce services may expose subjects to the possibility of harm without benefit.

Political or public policy agendas may exist that do not necessarily reflect the best interests of research subjects. If so, pharmacists must maintain the highest standards of integrity. This may require them to become more involved in establishing research priorities at federal, state, and local levels. We should address under what circumstances it is appropriate to encourage studies that are risky, potentially unfundable, or would require extensive time or commitment (which usually means a long delay before publishable results are generated). The probability of funding should not determine the direction of research.

Under what conditions is it permissible to delay the publication of promising results until more substantial evidence is available? The reverse question is an ethical dilemma as well. That is, under what conditions is it permissible to publish promising results even though, according to accepted standards, more evidence is needed to validate the results? The increasing newsworthiness of medical research has given this issue much attention, and conflicts directly with the established, albeit time-consuming, publication process: manuscript preparation, peer review, and revision.

Some have criticized the Ingelfinger rule.[11] Over a decade ago, the editor of the *New England Journal of Medicine*, Franz Ingelfinger, ruled that no medical research would be published if it had been published previously, whether in the scientific or lay press. (The rule permits previous publication of abstracts or presentations at meetings.) Most major scientific journals have similar policies.

Vocal patient groups, the lay press, and the public want medical news as fast as possible; results of new research are seen or heard daily in the news. The National Institutes of Health has begun releasing some research results (e.g., Clinical Alert) directly to health care providers and the public before the results are published. They deem the results too urgent for the public's health to be delayed by the publication process.[11] What are the ethical issues of such early release of research results, and who is the appropriate authority to decide what is urgent? How complete should the prepublication release of medical research be? What is the track record of prepublication releases? Is it unethical that some journals take months to print research results because of their peer review process? Policies should be developed that define appropriate mechanisms for early release of research findings, and their effectiveness and impact should be evaluated.

CLINICAL TRIAL DESIGN

The design of randomized clinical trials introduces ethical issues.[12] Usually, study designs prevent the treatment from being modified because of the need to collect sufficient data to allow valid statistical inference. Ethically, clinicians are required to provide their patients with the best available treatment; however, the justification for a randomized clinical trial is simply that the best treatment is not yet known.

What is the proper role for placebo controls? It has been suggested that, "apart from needing to be both valid and valuable,"[13] they must satisfy two premises: there exists (or there is the likelihood to exist) a controversy among expert clinicians concerning the relative therapeutic merits of each treatment, including the placebo; and the design of the study must warrant confidence that the results will show which of the regimens is superior and therefore will influence clinical practice.[13]

Placebo controls can be justified if the trial is conducted in an area that falls within one of four broad categories:

1. Conditions for which no standard therapy exists at all.
2. Conditions for which standard therapy has been shown to be no better than placebo.
3. Conditions for which standard therapy has been called into question by new evidence, creating doubt concerning its presumed net therapeutic advantage.
4. Conditions for which validated optimum treatment is not made freely available to patients because of cost constraints or other considerations (e.g., physical location of treatment centers).

These categories should be used as initial guidelines. The federal Food and Drug Administration desires that studies of a new chemical entity be compared with placebo in small groups of patients during phase II testing.

At what point should a clinical trial be stopped prematurely because enough evidence has been gathered to show that some treatment is efficacious? Investigators, with the help of statisticians, should develop guidelines that answer this question before the protocol is submitted to the IRB (or at least prior to data collection). These guidelines should be communicated to all persons involved in the research effort directly (investigators and research subjects). A safety committee should be responsible for monitoring data collected during a trial and stopping the trial if a predefined boundary is crossed, whether for early evidence of benefit or unacceptable toxicity.

INVESTIGATOR INDEPENDENCE

Investigator independence is another important issue. Almost all industry-funded research is reviewed by the sponsor prior to publication, and if the results are not favorable, pressure not to publish may be considerable. Some protocols forbid the investigator to publish results without permission; they cite the availability of confidential commercial information as the reason. The implied threat is that if the results are published, the investigator will not receive funding in the future. Pharmacists should be independent investigators with the right and authority to publish research findings. The intellectual property is owned by the investigators and their institution, not the funding agency.

SCIENTIFIC INTEGRITY

Integrity is a complex concept with associations to conventional standards of morality and personal beliefs about truth telling, honesty, and fairness. Unintentional investigator bias is a scientific error. Intentional investigator bias is a form of fraud. Fraud is the deliberate reporting of what one believes to be false with the intention of deceiving others.[14] Within a research program or institution, mechanisms should exist that check for data trimming, selective reporting, quality control, and originality. Sloppy research is unethical; examples are inconsistencies in record keeping involving research subject files, sample preparation and other analytical procedures, raw data files, and statistical analysis files. Plagiarism is another serious offense that compromises scientific integrity and is not acceptable.

Negative data should be published if they are scientifically sound, particularly when they fill gaps in current knowledge. They also may decrease redundancy in future investigations. Investigators should publish complete information when possible; fragmenting data sets is discouraged.

CONCLUSION

The research process introduces many ethical questions particularly relevant to clinical pharmacy investigators. Most important, investigators must be aware of their moral responsibility to safeguard the health and welfare of individuals who participate in research. The informed consent process is used to ensure that study subjects understand the conditions of their participation, the purpose of the study, and the possible hazards involved; and to ensure that consent is given freely. Investigators and IRBs must be certain that payments to study volunteers are not excessive or coercive. Finally, clinical pharmacist investigators must avoid or minimize potential conflicts of interest by establishing themselves as independent investigators performing studies with utmost scientific integrity.

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APPENDIX 1—THE NUREMBERG CODE[3,4]

1. The voluntary consent of the human subject is absolutely essential.
2. The experiment should be such as to yield fruitful results for the good of society, unprocurable by other methods or means of study, and not random and unnecessary in nature.
3. The experiment should be designed and based on the results of animal experimentation and a knowledge of the natural history of the disease or other problem under study that the anticipated results will justify the performance of the experiment.
4. The experiment should be so conducted as to avoid all unnecessary physical and mental suffering and injury.
5. No experiment should be conducted where there is a priori reason to believe that death or disabling injury will occur except, perhaps, in those experiments where the experimental physicians also serve as subjects.
6. The degree of risk to be taken should never exceed that determined by the humanitarian importance of the problem to be solved by the experiment.
7. Proper preparations should be made and adequate facilities provided to protect the experimental subject against even remote possibilities of injury, disability, or death.
8. The experiment should be conducted only by scientifically qualified persons. The highest degree of skill and care should be required through all stages of the experiment of those who conduct or engage in the experiment.
9. During the course of the experiment the human subject should be at liberty to bring the experiment to an end if he has reached the physical or mental state where continuation of the experiment seems to him to be impossible.
10. During the course of the experiment the scientist in charge must be prepared to terminate the experiment at any stage, if he has probable cause to believe, in the exercise of the good faith, superior skill, and careful judgment required of him that a continuation of the experiment is likely to result in injury, disability, or death to the experimental subject.

APPENDIX 2—MAJOR COMPONENTS OF THE WORLD MEDICAL ASSOCIATION DECLARATION OF HELSINKI[5]

E

Basic Principles

1. Biomedical research involving human subjects must conform to generally accepted scientific principles and should be based on adequately performed laboratory and animal experimentation and on a thorough knowledge of the scientific literature.
2. The design and performance of each experimental procedure involving human subjects should be clearly formulated in an experimental protocol which would be transmitted to a specially appointed independent committee for consideration, comment, and guidance.
3. Biomedical research involving human subjects should be conducted only by scientifically qualified persons and under the supervision of a clinically competent medical person. The responsibility for the human subject must always rest with a medically qualified person and never rest on the subject of the research, even though the subject has given his or her consent.
4. Biomedical research involving human subjects cannot be legitimately carried out unless the importance of the objective is in proportion to the inherent risk to the subject.
5. Every biomedical research project involving human subjects should be preceded by careful assessment of predictable risks in comparison with foreseeable benefits to the subject or to others. Concern for the interest of the subject must always prevail over the interest of science and society.
6. The right of the research subject to safeguard his or her integrity must always be respected. Every precaution should be taken to respect the privacy of the subject and to minimize the impact of the study on the subject's physical and mental integrity and on the personality of the subject.
7. Doctors should abstain from engaging in research projects involving human subjects unless they are satisfied that the hazards involved are believed to be predictable. Doctors should cease any investigation if the hazards are found to outweigh the potential benefits.
8. In publication of the results of his or her research, the doctor is obliged to preserve the accuracy of the results. Reports of experimentation

not in accordance with the principles laid down in the Declaration should not be accepted for publication.

9. In any research on human beings, each potential subject must be adequately informed of the aims, methods, anticipated benefits, and potential hazards of the study and the discomfort it may entail. He or she should be informed that he or she is at liberty to abstain from participation in the study and that he or she is free to withdraw his or her consent to participation at any time. The doctor should then obtain the subject's freely given informed consent, preferably in writing.
10. When obtaining informed consent for the research project the doctor should be particularly cautious if the subject is in a dependent relationship to him or her or may consent under duress. In that case the informed consent should be obtained by a doctor who is not engaged in the investigation and who is completely independent of this official relationship.
11. In case of legal incompetence, informed consent should be obtained from the legal guardian in accordance with national legislation. Where physical or mental incapacity makes it impossible to obtain informed consent, or when the subject is a minor, permission from the responsible relative replaces that of the subject in accordance with national legislation.
12. The research protocol should always contain a statement of the ethical considerations involved and should indicate that the principles enunciated in the present Declaration are complied with.

Medical Research Combined with Professional Care (Clinical Research)

1. In the treatment of the sick person, the doctor must be free to use a new diagnostic and therapeutic measure, if in his or her judgment it offers hope of saving life, reestablishing health, or alleviating suffering.
2. The potential benefits, hazards, and discomforts of a new method should be weighed against the advantages of the best current diagnostic and therapeutic methods.
3. In any medical study, every patient—including those of a control group, if any—should be assured of the best proven diagnostic and therapeutic method.
4. The refusal of the patient to participate in a study must never interfere with the doctor–patient relationship.
5. If the doctor considers it essential not to obtain informed consent, the specific reasons for this proposal should be stated in the experimental protocol for transmission to the independent committee.
6. The doctor can combine medical research with professional care, the objective being the acquisition of new medical knowledge, only to the extent that medical research is justified by its potential diagnostic or therapeutic value for the patient.

Nontherapeutic Biomedical Research Involving Human Subjects (Nonclinical Biomedical Research)

1. In the purely scientific application of medical research carried out on a human being, it is the duty of the doctor to remain the protector of the life and health of that person on whom biomedical research is being carried out.
2. The subjects should be volunteers—either healthy persons or patients for whom the experimental design is not related to the patient's illness.
3. The investigator or the investigating team should discontinue the research if in his or her or their judgment it may, if continued, be harmful to the individual.
4. In research on man, the interest of science and society should never take precedence over considerations related to the well-being of the subject.

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European Society of Clinical Pharmacy

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INTRODUCTION

In the 20th century, a conviction developed within the pharmacy profession that the professional knowledge of pharmacists was not used to its full potential. Activities to assure the safe and appropriate use of drugs became a new target, leading to activities in the direction of more patient-related aspects of drug therapy. This perception was present at about the same time on both sides of the Atlantic. It was logically named "Clinical Pharmacy," meaning a pharmacy activity directed to and in contact with the patient. The leaders of this new approach wanted to reinforce their message by founding professional organizations preoccupied with the teaching and practical development of Clinical Pharmacy. In 1979, the birth of the American College of Clinical Pharmacy (ACCP) and the European Society of Clinical Pharmacy (ESCP) took place simultaneously.[1]

WHAT IS ESCP?

The European Society of Clinical Pharmacy (ESCP) is an international society founded by clinical practitioners, researchers, and educators from various countries in Europe, which constantly looks for new areas of professional practice. Since the formation of the Society, there has been a gradual and sustained growth of clinical pharmacy in many European countries.

Overall Aim

The overall aim of the Society is to develop and promote the rational and appropriate use of medicines (medicinal products and devices) by the individual and by society.

Goal

The goal of ESCP is to encourage the development and education of clinical pharmacists in Europe.

The Society tries to achieve this goal by:

1. *Membership activities*:
   - Providing a forum for the communication of new knowledge and developments in clinical pharmacy.
   - Developing links with national and international organizations of pharmacists, teachers, and students interested in the development of clinical pharmacy.
2. *External relations*:
   - Promoting the value of clinical pharmacy services among other health care professionals, among scientific societies that share the same interest, organizations such as WHO (World Health Organization) and EMEA (European Agency for the Evaluation of Medicinal Products), and generally within the health service.
3. *Educational activity*:
   - Enforcing the formation of activities in the field of clinical pharmacy and pharmacotherapy through conventions and specific courses.
   - Promoting the inclusion of clinical pharmacy teaching at pre- and postgraduate levels.
4. *Training*:
   - Providing accrediting centers, where clinical pharmacy activities are carried out and which are prepared to host visiting pharmacists or pharmacy students in each European country.

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5. *Research*:
   - Promoting multicenter research in all areas of clinical pharmacy.
   - Promoting the participation of pharmacists in clinical trials and pharmacoeconomic studies.
6. *Publications*:
   - Producing a number of publications on clinical pharmacy.
   - Promoting a more widespread use of existing clinical pharmacy publications.

CLINICAL PHARMACY

Clinical pharmacy is a health specialty, which describes the activities and services of the clinical pharmacist to develop and promote the rational and appropriate use of medicinal products and devices.

Clinical pharmacy includes all the services performed by pharmacists practicing in hospitals, community pharmacies, nursing homes, home-based care services, clinics, and any other setting where medicines are prescribed and used.[2]

Activities of the clinical pharmacist are consulting, selecting drugs, providing drug information, formulating and preparing medicinal products and devices, conducting drug use studies/pharmacoepidemiology/outcome research/pharmacovigilance and vigilance in medical devies, studying pharmacokinetics/therapeutic drug monitoring, conducting clinical trials, being aware of the pharmacoeconomy, dispensing and administrating medicinal products and devices, and providing pre- and postgraduated teaching and training activities to provide training and education programs for pharmacists and other health care practitioners.[1,3]

ACTIVITIES OF ESCP

To obtain the goals and objectives, ESCP organizes different types of activities.

Conferences and Symposia

Every year in autumn, the Society's European Symposium on Clinical Pharmacy is held. ESCP also organizes Spring Conferences, focused on specific themes to provide professional education. During these conferences, workshops play an important role.

Education and Research

On the day prior to the Annual Symposium, ESCP organizes a one-day full immersion course, "Masterclass in Search of Excellence," on specific topics of interest. ESCP and EPSA (European Pharmaceutical Students' Organization) jointly organize a Students' Symposium, which aims to bring the clinical pharmacists and pharmacy students together to learn from each other's perspectives and experiences.

Different educational and research programs have been developed and are planned for the coming years (see ESCP Calendar of Events mentioned below and at www.escp.nl).

Several collaborative studies, particularly in the field of drug utilization review and drug evaluation, among member countries have been or are still in progress.

ESCP offers awards to individual researchers in clinical pharmacy fields in collaboration with sponsors.

A number of accredited centers have been established to enable European clinical pharmacists to gain experience in a range of clinical pharmacy specialties.

ESCP has produced a database of clinical pharmacy courses in Europe. Moreover, a long distance Pharmacotherapy Self-Assessment Program (PSAP) published by ACCP is available at ESCP.

Publications

The editing and issuing of publications and journals is an important task undertaken by ESCP and comprises the publication of the *Proceedings of the Annual Symposium in Pharmacy World and Science* (PWS). The Society has adopted a scientific journal *Pharmacy World and Science*, where research papers are published and are retrievable.

ESCP Newsletter is a bimonthly publication, serving as a link between the Society and their members, with news about the activities of ESCP and of the members.

In addition, ESCP selects existing clinical pharmacy publications for promotion among ESCP members.

Related Organizations

To promote the value of clinical pharmacy services among other health care professionals and scientific societies, ESCP has established a relationship with societies that share the same interests: American College of Clinical Pharmacy (ACCP), American Society for Health Care Systems (ASHP), European Association of Hospital Pharmacists (EAHP), European Pharmaceutical Students'

Association (EPSA), Royal Dutch Association for the Advancement of Pharmacy (KNMP), and the United Kingdom Clinical Pharmacy Association (UKCPA). ESCP has been recognized by the Efficacy Working Party of the European Agency for the Evaluation of Medicinal Products (EMEA) as contributor in the consulting process. Within the European Forum of Pharmaceutical Associations and the World Health Organization Regional Office for Europe (EuroPharm Forum), ESCP is recognized as an observer organization.

ORGANIZATION OF ESCP

The European Society of Clinical Pharmacy International Office is located at Theda Mansholtstraat 5b, 2331 JE Leiden, The Netherlands (Phone: +31 (0)71 5722430; Fax: +31 (0)71 5722431; E-mail: office@escp.nl; Internet: www.escp.nl).

General Committee

The Society is conducted by a General Committee consisting of 12 members. They represent individual countries or, where appropriate, groups of countries. General Committee members are elected by the membership. The General Committee meets twice a year, before the Annual Symposium and Spring Conference. (See Table 1 for more information about the General Committee.)

Executive Committee

The General Committee elects the Executive Committee, which implements the resolutions passed by the General Committee and by the General Assembly. The Executive Committee, composed of the President, Past-President, Vice-President, Treasurer, and Chair of the Research and Education Committee is responsible for the day-to-day coordination of ESCP activities.

Table 1 General committee members 2001–2002

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Research and Education Committee

The Research and Education Committee is in charge of the coordination of educational activities, stimulates and initiates research project, and takes care of the scientific level of these activities.

Special Interest Groups

The Special Interest Groups (SIGs) of ESCP are intended to help ESCP meet the evolving needs of its members and fulfill a growing need for providing targeted services to ESCP members with similar interests.

The goal is to provide a focal point to gather ESCP members with common interests and needs in practice, research, and education, to create a network for:

- Professional interaction.
- Problem solving and discussion of professional issues.
- Continuing education.
- Research.
- Publications.

The following SIGs are currently active: Cancer Care, Drug Information, Education and Training, Geriatrics, Infectious Diseases, Integrated Primary Care, Nutritional Support, Pediatrics, Pharmacoeconomics, Pharmacoepidemiology, and Pharmacokinetics.

International Office

The Society has an International Office which coordinates the total operations of the Society, administers the activities of the Society, and implements new policies and strategies. The staff of the International Office consists of a director, who is a pharmacist, and two secretaries. The director of the ESCP International Office is Annemieke Floor-Schreudering.

Members

ESCP has about 850 members from 48 countries. Members practice in hospitals, clinics, universities, community pharmacies, governmental settings, drug information centers, pharmaceutical industry, and any other places where clinical pharmacists are employed. The Society has four different classes of members: *ordinary members* are individuals who are actively involved in pursuing the objectives of the Society; *honorary members* are those who have distinguished themselves in a particularly honorable way toward the Society; *patrons and sponsors* are individuals or corporate bodies, who have expressed their willingness to support the Society financially; and *student members* are individual students or educational institutions.

During its Annual Symposium, ESCP holds a General Assembly for all members and patrons of the Society.

CALENDAR OF EVENTS

October 2002	Florence, Italy	31st European Symposium on Clinical Pharmacy
May 2003	Portugal	4th Spring Conference on Clinical Pharmacy

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Evidence Based Practice

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INTRODUCTION

In 1992, a group led by Gordon Guyatt at McMaster University in Canada[1] first articulated the term "evidence based medicine." Evidence-based medicine (EBM) was defined more recently as "the integration of best research evidence with clinical expertise and patient values."[2] Despite its recent recognition, EBM has probably always been practiced by health professionals, but what has changed is that the quality of evidence and the clinical benefit of applying it, are now looked at critically and systematically.

Historically, personal experience, the advice of a professional colleague or data presented in an article in a health journal might have been considered sufficient evidence on which to base a clinical decision. Nowadays, the importance of using "best evidence" to underpin practice is recognized, thereby increasing the likelihood that an effect can be predicted with confidence. The growth in EBM has been accompanied by a greater understanding of the different levels of evidence.

The demand for healthcare increases relentlessly, therefore, it is essential that decision makers operate at both patient and population levels within an evidence-based framework. Evidence is needed for diagnostic tools, management options (including drug treatments), the introduction of healthcare models, and patients' values regarding their health service. Scarce resources should not be spent on treatments which provide little benefit or which may even do harm. The relative effectiveness of treatments needs to be assessed where there is competition for limited resources. Valid and reliable information on the clinical and cost-effectiveness of different options is therefore needed.

Another reason for the need for EBM is the accelerating pace with which new procedures and treatments are introduced, with the result that knowledge gained during training quickly becomes redundant. It is essential, therefore, to have up-to-date information about best clinical practice.

This article describes how to find and understand the evidence, and how to apply it in the healthcare setting.

FINDING THE EVIDENCE

The first stage in practicing EBM is to define the precise question to which an evidence-based answer is required. A carefully focused question will inform the search for relevant evidence, and should (hopefully) avoid excessive retrieval of irrelevant publications and other information sources. For example, a clinician who wishes to know whether it is best to use oral or topical antifungals for the treatment of vaginal candidiasis could articulate the question as "What is the relative effectiveness of oral versus intra-vaginal antifungals for the treatment of uncomplicated vulvovaginal candidiasis?"

There is a hierarchy[3] of trial evidence:

- Ia Evidence obtained from meta-analysis of randomized controlled trials.
- Ib Evidence obtained from at least one randomized controlled trial.
- IIa Evidence obtained from at least one well-designed controlled study without randomization.
- IIb Evidence obtained from at least one other type of well-designed quasi-experimental study.
- III Evidence obtained from well-designed nonexperimental descriptive studies, such as comparative studies, correlation studies, and case studies.
- IV Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities.

The above ranking depends not only on the type, but also the quality of the studies. Therefore, a badly conducted randomized controlled trial could be less robust than a well-conducted controlled clinical trial.

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Table 1 Quality "questions" for assessing RCTs

- Were subjects randomly assigned to treatment?
- Was randomization done blindly?
- Were all subjects analyzed?
- Was analysis according to unit of randomization?
- Were researchers blind to group allocation?
- Apart from the intervention, were the two groups treated equally?
- Were the groups similar at baseline?

It is important to ensure that all the relevant information is identified and critically appraised. This is easier said than done! Evidence that is unpublished or that is not in the public domain is difficult to identify and retrieve. Pharmaceutical companies might not publish unfavorable results of drug trials, therefore, the clinician or reviewer is reliant upon the cooperation of the company to provide all relevant trial data for its specific drug. Trials reported in the English language[4] and those with positive outcomes are more likely to be published. Problems can also arise if trial results have been accepted by a medical journal that has a long time lag before publication. It may be months or years before the results are published. The sources and avoidance of bias are discussed elsewhere. It is important to attempt to minimize the effects of bias when reviewing evidence. It is also useful to contact experts on the subject of interest, as they will be able to advise on sources of relevant data and contact details of researchers conducting trials in the area. Other useful methods of identifying potentially relevant information include placing notices about the literature review in professional journals and on web site noticeboards and searching conference abstracts and lists of grant awards.

Once the literature search is complete, the identified trials need to be retrieved and reviewed critically to decide whether they satisfy specific standards for inclusion in the review. A list of some important quality criteria for randomized controls is shown in Table 1. It is essential that studies that do not meet the necessary quality standards be excluded from the final analysis.

UNDERSTANDING THE EVIDENCE

The results of trials can be used for different purposes. They could be combined and reviewed descriptively, or, if

Table 2 Relative risk

	Outcome		
	Yes	No	Total
Drug A	a	b	a + b
Drug B	c	d	c + d

Where,

a = the number of subjects receiving Drug A with the outcome

b = the number of subjects receiving Drug A without the outcome

c = the number of subjects receiving Drug B with the outcome

d = the number of subjects receiving Drug B without the outcome

If the outcome was cure then the relative risk of cure would be calculated as follows:

The risk of cure with Drug A = a / a + b,

divided by the risk of cure with Drug B = c / c + d

with Drug

B = c / c + d.

	Outcome		
	Yes	No	Total
Durg A	10	20	30
Durg B	5	50	55

Relative risk = (a / a + b) ÷ (c / c + d) = (10 / 30) ÷ (5 / 55) = 3.7

This means that cure is 3.7 times more likely with Drug A than Drug B.

Table 3 Number needed to treat

Absolute risk reduction (ARR) = (a/(a + b)) − (c/(c + d))
For the above example, using the hypothetical values in Table 2, ARR = (10/(10 + 20)) − (5/(5 + 50)) = 0.24
Therefore, the NNT = 1/0.24 = 4
This means that for every four people treated with Drug A, one additional cure is likely to occur.

the trials are similar enough, their data can be combined in the form of a meta-analysis. This technique allows reporting the results to a greater level of statistical confidence because of the increased numbers of subjects included in the analysis.

An alternative statistic which is sometimes quoted is the odds ratio (OR). This is the odds of an event occurring in a patient in one treatment group relative to the odds of the same event occurring in a patient in an alternative treatment group.

The results of randomized controlled trials comparing two drugs can be used to generate a statistic called the relative risk (RR) (Table 2). This is a ratio of the risk of an outcome with one treatment and the risk of the same outcome with the other treatment.

While the relative risk is a standard statistic that can be used to compare treatments, it can be difficult to understand and to relate to practice. For example, although the relative risk of 3.7 that was calculated above indicates that Drug A is associated with nearly four times the risk of cure compared with Drug B, this gives no indication of the practical implications. For this reason, effects are often quoted as the "Number Needed to Treat" (NNT). The NNT is calculated as the reciprocal of the absolute risk reduction (ARR). In the example in Table 3, the NNT refers to the number of patients who need to receive Drug A before an additional cure is likely to occur.

APPLYING THE EVIDENCE

Having identified the evidence from the available information and interpreted it in the context of the original question, the next step is to apply it to practice. This is a complex and challenging task. The evidence may suggest benefits from discontinuing existing treatments or changing to alternative therapy, e.g., using a beta-blocker in hypertensive patients following a myocardial infarction.[5] Alternatively, the evidence may recommend against adopting a new "miracle" drug such as the anticholinesterase inhibitors for Alzheimer's disease.[6]

Currently, much clinical practice is based on established practice and personal experience. Producing changes in practice will involve the dissemination of information to individual clinicians and persuading them that, sometimes against their better judgment, there is a benefit in adopting a new approach. Evans and Haines[7] cite 12 initiatives to introduce evidence-based practice, and they are refreshingly honest in identifying the barriers that are encountered. These included the time required to support change; the resources needed from existing budgets; a failure to always demonstrate quantifiable gains in the real world; a failure to give ownership to all parties; and, probably the most difficult and complex of all, changing professional behavior. This last area is a research topic in its own right and is discussed later in this article.

Patient resistance to change, as well as professional resistance, also needs to be addressed. For example, new evidence may require changes to be made to a patient's current long-term medication. Patients previously satisfied with their treatment may be reluctant to try a new drug, despite evidence of greater benefit. A concordant and patient-centered approach is being promoted.[8] The clinician has a responsibility to involve their patients in treatment decisions and to ensure that they understand and agree with any changes that are made, as well as address any concerns that they may have. In the interests of maximizing patient outcomes and cost-effective use of medicines, it is paramount that patients understand and agree with new or existing treatments. Within this framework, management decisions may not be in line with current best evidence, giving rise to a debate about the legal implications and professional ethical issues of this scenario.

It is important to remember that EBM applies to a range of providers at a variety of levels. Thus, it should be used to support decision making by all healthcare providers, not just medical clinicians. It is for this reason that the term Evidence-Based Practice (EBP) is increasingly used. Pharmacy, nursing, physiotherapy, and all other professions allied to medicine should, where possible, be providing evidence-based treatment at an individual and service level. For example, evidence can support decisions about whether to treat stroke patients in a dedicated stroke unit or as part of a general ward.[9]

CRITICISMS OF EVIDENCE-BASED MEDICINE

There are two levels of criticism applied to evidence-based medicine. The first relates to the widespread dependence on the randomized controlled trial, and the second relates to the patient–population dichotomy.

Concern has been expressed that gold standard evidence, i.e., the RCT, may not be as robust as it first appears. Critics of this study design argue that the patient populations are highly selected. Randomized controlled trials often exclude patients above a certain age or those who are taking other concomitant medications or who have significant comorbidities. Additionally, participants in RCTs often have intensive support from medical, nursing, and research staff, contrary to the normal situation. The reasons for these exclusions and enhanced care are self-evident, but they may mean that the results are not generalizable to the wider patient population. A comparison of randomized and nonrandomized studies has also identified that subjects excluded from RCTs tend to have worse prognosis than those who are included.[10] Furthermore, subjects entered into RCTs for evaluation of treatment for existing conditions may be less affluent, less educated, and less healthy then those who are not. The opposite is true for trials of preventive interventions.[10]

Secondly, clinicians have argued that evidence-based guidelines do not accommodate individual patients and their specific circumstances or needs. It may be necessary to remind clinicians that guidelines "are not tramlines"—they apply to a specific population, and their recommendations should be tailored to the needs of their individual patients. This is discussed later in this article.

CHALLENGES OF BASING DECISIONS ON EVIDENCE AT POLICY AND INDIVIDUAL PATIENT LEVELS

With increasing healthcare costs, particularly in the field of drug treatments, decisions regarding the uptake of new drugs may be made at organizational rather than individual clinician or patient level. In the United Kingdom, this is particularly true in areas where NHS budgets constrain both the choice of treatment and patient selection. EBM can be used to inform these policy decisions, as it can assess both the cost-effectiveness and clinical effectiveness of treatments. The final decision can take into account the wider ramifications of alternative treatments, such as the possible need for residential or surgical care or the impact on lay carers. A decision may be made at a population level that a new drug should not be introduced because of the adverse overall health economic balance, whereas at an individual level, it could be worth trying.

An example of this patient versus the population dilemma is illustrated by the use of the expensive interferon-beta-1b to treat secondary progressive multiple sclerosis (MS). The evidence tells us that treatment with interferon-beta-1b will delay time to wheelchair dependence and prevent relapses in some subjects. However, the NNT is 18 and at a population level, the economics mitigate against making this a recommended treatment.[11] Conversely, despite their cost, there has been considerable use of statins as lipid-lowering agents to reduce cholesterol levels in targeted patients.[12] This is because the evidence shows long-term reduction in further coronary events, and the exact health gain can be calculated and is deemed worthwhile.[13] This intervention is both clinically and cost effective.

Ultimately, it is the clinician who has to weigh the costs and benefits for each individual patient, taking into account the evidence but also considering patient factors. This has been summarized as "conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients."[14]

WHAT TO DO WHEN THERE IS NO EVIDENCE OR EVIDENCE IS INCOMPLETE

The EBM movement is a relatively recent endeavor. With such a wide range of treatments available and numerous conditions, it is inevitable that there will not always be evidence to inform decision making. This may be due to a lack of collation of the available research evidence or a lack of research per se. In these instances, there are several options depending on the immediacy of the decision.

If a decision needs to made quickly, advice should be sought from the most experienced practitioner on the subject. This advice should be interpreted with caution and considered in light of whatever published literature exists. This should be judged on the basis of the ranked levels of evidence included earlier in this article. New drugs may be tried in the context of local clinical trials. If this is the case, these trials should be expertly designed and conducted in collaboration with other colleagues. This means that while a treatment may not ultimately be the best, it will have been used in a controlled way such that it has contributed to generating future evidence.

CLINICAL EFFECTIVENESS AND CLINICAL GOVERNANCE

There is a growing emphasis on the accountability of individual clinicians and organizations that provide

healthcare. EBM contributes to the definition of criteria used for clinical performance indicators. This forms the basis of assessing the clinical effectiveness of services. Increasingly, clinicians and their corporate managers are held responsible for the delivery of quality care; this is known as clinical governance. Despite the caveats for EBM summarized above, the knowledge and understanding it has promoted now underpin the healthcare infrastructures that exist today.

THE PHARMACIST'S ROLE

Pharmacists can contribute to the delivery of evidence-based care.[15] At a population level, pharmacists' clinical knowledge and analytical strengths can be used to facilitate the production of systematic reviews, the interpretation and analysis of findings, and the development of guidelines. At a patient level, pharmacists are consulted in both primary and secondary care, and may be a useful vehicle for transfer of evidence-based information to the clinician, being able to give a more objective decision than the doctor faced with a patient with alternative expectations.[16] Pharmacists can influence the choice of prescribed drugs mediated either through the GP to the patient, or face to face with the patient.[17]

In many countries, a wider range of drugs is available for purchase from pharmacies without the need for a prescription. This has enabled pharmacists to provide treatment and advice for a greater range of minor illnesses. Although there have been concerns that pharmacists and their staff may give inappropriate advice,[18–21] the use of evidence-based guidelines to support their treatment of minor illness is currently being explored.[22]

RESOURCES FOR EVIDENCE-BASED MEDICINE

Electronic databases of peer-reviewed healthcare journals (primary references) include MEDLINE and EMBASE. The Cochrane Collaboration library contains a database of systematic reviews as well as a database of RCTs and controlled clinical trials. Medical librarians will be able to advise and perhaps provide training on performing literature searching and retrieval. Hospital-based drug information centers will likely have access to a range of electronic databases. The Royal Pharmaceutical Society of Great Britain's information center has a number of databases that can be searched for information that is of particular relevance to drug therapy and pharmaceutical care. It is likely that most national pharmaceutical organizations have similar resources.

One of the greatest resources for EBM is the World Wide Web. There are numerous sites that provide information on EBM, including literature retrieval and review, EB guidelines, and so on (Table 4).

GETTING EVIDENCE INTO PRACTICE: DISSEMINATION AND IMPLEMENTATION

The mere dissemination of information (i.e., evidence) is unlikely to achieve behavioral change.[23] In order for evidence to influence practice, active dissemination and implementation strategies need to be employed. It is recognized that "individual beliefs, attitudes and knowledge influence professional behavior" and that "other factors including organisational, economic and community environments of the practitioner are also important."[24] It has been suggested that implementation strategies that

Table 4 Suggested EBM-related web sites

Adept Programme	www.shef.ac.uk/~scharr/ir/adept
Agency for Healthcare Research and Quality (USA)	www.ahcpr.gov/
Bandolier	www.jr2.ox.ac.uk/bandolier/
Critical Appraisal Skills Programme	www.phru.org.uk/~casp/index.htm
National Guideline Clearing (USA)	www.guideline.gov/index.asp
Netting the Evidence	www.shef.ac.uk/~scharr/ir/netting/
NHS Centre for Evidence-Based Medicine	www.minervation.com/cebm/
National Institute for Clinical Excellence (UK)	www.nice.org.uk
Primary Care Clinical Practice Guidelines	www.medicine.ucsf.edu/resources/guidelines/
Scottish Intercollegiate Guidelines Network (SIGN)	www.sign.ac.uk
The NHS Centre for Reviews and Dissemination	www.york.ac.uk/inst/crd/welcome.htm
TRIP Database	www.tripdatabase.com/index.cfm
UK Cochrane Centre	www.cochrane.org/
Virtual library	www.shef.ac.uk/~scharr/ir/core.html

address barriers to change may be more effective than those that do not.[24] A comprehensive review of implementation strategies is presented in the *Effective Health Care Bulletin: Getting Evidence Into Practice*.[24]

The use of guidelines as a method of summarizing evidence is discussed elsewhere in this encyclopedia. There has been considerable evaluation of the effectiveness of different guideline implementation strategies as methods of eliciting behavior change among healthcare professionals. Most implementation research has targeted physician behavior. However, as greater emphasis is placed on multidisciplinary healthcare teams, strategies need to be identified, tested, and adopted, which are effective in promoting evidence-based practice among all health professional groups.

Mass media is a method commonly used to disseminate information to large audiences. This strategy usually involves the dissemination of printed materials (e.g., guidelines, therapeutic bulletins) to specific health professionals (e.g., physicians, pharmacists). There is little evidence to support the use of this method, as it is largely ineffective in influencing behavior change.[25]

Educational outreach visits (also known as academic detailing) have been used by the pharmaceutical industry for decades to influence the prescribing behavior of physicians. Although there is little published empirical evidence of the effect of the pharmaceutical industry's promotional activities on prescribing patterns, the investment of 57% of their pharmaceutical promotion budget on pharmaceutical representatives and 11% on promotional literature, gives some indication of its importance.[26] There is considerable research evidence of the effectiveness of educational outreach as a behavior change strategy for healthcare professionals.[27] It is no surprise (considering their origin) that educational outreach visits have been shown to be effective in achieving change in prescribing behavior among physicians.[27]

The use of opinion leaders as an implementation strategy has been evaluated in a number of studies, the results of which are inconclusive.[28] This method relies on persuasion (i.e., the persuasive ability of the opinion leader) to influence the behavior of the target audience. Further evaluation of this strategy is required, including methods of describing characteristics of opinion leaders and how to identify individuals who satisfy these criteria.

SUMMARY

Evidence-based practice is increasingly recognized as the best way to maximize the chances of individual patients receiving the most appropriate treatment. It is also used to inform policy making about both medical treatments and new services, including models of healthcare.

While there are still some caveats, some of which have been highlighted in this article, EBP is the goal to which all healthcare professionals should aspire.

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PROFESSIONAL DEVELOPMENT

Fellowships in Pharmacy

F

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INTRODUCTION

The term *fellowship* is used to designate training programs or to indicate status within a profession or professional organization. In pharmacy, the accepted definition for a fellowship is "a directed, highly individualized, postgraduate program designed to prepare the participant to become an independent researcher." This definition was adopted by a coalition of seven national pharmacy organizations to distinguish fellowship from residency training.[1] This definition is contrasted with that for a *residency* which is "an organized, directed, postgraduate training program in a defined area of pharmacy practice." Training fellowships may occur at any stage of education and are commonly referred to as *predoctoral* (usually at the undergraduate level) or *postdoctoral* (*postgraduate*). This article includes discussion of fellowship as a postdoctoral research training program.

DEFINITIONS

A member of a professional organization may be designated as a fellow to recognize accomplishments, experience, or some other laudable standing in the profession. For example, a person may be a Fellow of the American College of Clinical Pharmacy (ACCP) or the American Society of Health-System Pharmacists (ASHP). This designation does not indicate completion of a training program nor proficiency in research.

Fellowships are offered by many institutions, including colleges and universities, government entities such as the National Institutes of Health and the Centers for Disease Control and Prevention, pharmaceutical manufacturers, healthcare systems, and professional organizations. Most pharmacy fellowship training programs are offered by colleges of pharmacy or academic medical centers.

Generally, fellowships are generally highly individualized programs to develop competency in research, including conceptualizing a research problem, planning and conducting research processes and experiments, analyzing data, and reporting of results. These programs are conducted under the close supervision of an experienced research mentor or preceptor. More so than most residencies, a fellowship is guided by one person or a small group of individuals. Fellowships are generally 12 or 24 months in duration and fellows often complete formal courses in selected topics such as research design, statistics, or research methods before or during a fellowship. Fellows should possess basic pharmacy practice skills relevant to the knowledge area of the fellowship. These skills are acquired through training in a Pharm.D. program, a residency, or practice experience. For most individuals, a residency should be completed before beginning a fellowship.

The goal of fellowship training is to produce an individual capable of conducting collaborative research or functioning as a principal investigator. A fellowship-trained individual will usually work for a college of pharmacy, academic medical center, pharmaceutical company, or contract research organization. Research-intensive positions often indicate a hiring preference for those with fellowship training.

GUIDELINES FOR CLINICAL FELLOWSHIP TRAINING PROGRAMS

In 1987 a document with specific guidelines for clinical fellowship training programs in pharmacy was approved by ACCP and the American Association of Colleges of Pharmacy.[2] The guidelines, which have been updated by ACCP, relate to the training program overall, preceptor qualifications, fellow qualifications, and the fellowship experience, as follows.

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Training Program Requirements

1. In general, a commitment of 80% of fellowship training time to research activities over a period of at least two years.
2. Administrative institutional support for the preceptor's research program and the fellowship training program.
3. Availability of graduate-level course work in the area of the fellowship.
4. Availability of personnel to teach laboratory-based and clinical research skills.
5. Ready access to a medical library and computer facilities.

Preceptor Qualifications

1. A clinical scientist with an established record of research accomplishments, which may be exemplified by:
    a. Fellowship training or equivalent experience.
    b. Principal or primary investigator on research grants.
    c. Published research papers in peer-reviewed pharmacy/medical literature where the preceptor is primary or senior author.
2. Active collaborative research relationships with other scientists.
3. Expertise in pharmacotherapeutics in the area of specialization.

Fellowship Applicant Requirements

1. Pharm.D. or equivalent experience.
2. Residency or equivalent experience.
3. High level of motivation for a research career.

Fellowship Experience

The initiation and completion of a research project, including:

1. Development of at least one scientific hypothesis and experimental methods to test hypothesis.
2. Preparation and submission of a grant proposal.
3. Submission of a protocol to the appropriate institutional review committee.
4. Research experiences including study conduct and data collection related to the field of specialization.
5. Experience in statistical analysis of data.
6. Preparation and submission of abstracts and manuscripts for publication in peer-reviewed journals.
7. Formal presentation of research at peer-reviewed scientific meetings.
8. Participation in journal clubs, research workshops, and seminar series.
9. Instruction in biomedical science ethics.

REVIEW OF FELLOWSHIPS

In an effort to improve fellowship training, ACCP instituted a program for peer review of research fellowships training programs to assure quality of these programs. This is a voluntary process conducted by an ACCP committee to determine whether a program meets the ACCP Guidelines for Research Fellowship Training Programs as detailed above. In this process, both the preceptor and the fellowship site are evaluated. A positive review indicates that the program meets the guidelines. At present, 15 fellowship programs have been recognized as meeting the guidelines.[3]

FELLOWSHIP RESOURCES

An excellent resource for information about pharmacy fellowships is the ACCP Directory of Residencies and Fellowships.[3] This source provides information on over 100 individual fellowship programs. Additional information on fellowships can be obtained from the Academy of Managed Care Pharmacy[4] and the American Pharmaceutical Association.[5] Currently, fellowships can be served in the following areas:

- Ambulatory care.
- Cardiology.
- Clinical pharmacology.
- Critical care.
- Drug development.
- Drug information.
- Family medicine.

- Geriatrics.
- Infectious diseases.
- Internal medicine.
- Managed care pharmacy.
- Nephrology.
- Neurology.
- Oncology.
- Outcomes research.
- Pediatrics.
- Pharmacoeconomics.
- Pharmacoepidemiology.
- Pharmacokinetics.
- Psychiatry.
- Pulmonary.
- Rheumatology.
- Translational research.
- Transplantation.

Funding for fellowships varies from year to year and has been available from pharmacy organizations including ACCP, ASHP, American Society of Consultant Pharmacists, and the American Foundation for Pharmaceutical Education.

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INTRODUCTION

Successful computerization and drug-related decision support is achieved to a significant degree within the profession of pharmacy. Pharmacy has been a leader among healthcare professions in embracing computerization. Drug databases and knowledge bases are now the backbone of pharmaceutical care or pharmaceutical decision support.

MISSION STATEMENT

Our mission is to be the best provider of point-of-care decision support knowledge bases that provide outstanding value to patients and to our customers. We are committed to exceeding our customers' expectations so that they regard us as the best company in our industry. We will achieve this position through the comprehensiveness and quality of our data, the responsiveness of our service, and our understanding of their business problems. While continuing to grow, we will provide an open, supportive, challenging, and team-oriented environment within which our staff members can achieve job satisfaction, professional and personal growth, and compensation based on company and individual performance. We will actively work to increase our impact on the quality of healthcare.

First DataBank is one of the world's leading suppliers of healthcare knowledge bases, supplying drug knowledge bases, as well as medical diagnostic and nutrition software to system vendors. First DataBank serves hospitals, hospital pharmacies and laboratories, retail pharmacies, physician clinics and group practices, insurers, managed care organizations, pharmacy benefits managers, claims processors, employers, utilization review organizations, government, pharmaceutical manufacturers, wholesalers, and all 50 state Medicaid programs.

First DataBank's professional staff is committed to deliver comprehensive and accurate information to physicians, pharmacists, nurses, dietitians, and other healthcare professionals to be useful in a variety of healthcare settings. Drug information to be used directly by consumers (i.e., patients and their families) is also another focus of our drug knowledge bases. These knowledge bases are updated continually and are available to accommodate any update schedule, providing the immediate access that businesses need to perform mission critical functions and to realize significant time and financial savings. Enhancements in the delivery of pharmaceutical care have increased the need for First DataBank to deliver clinically significant drug information in a timely manner. Therefore, updates to products containing clinical knowledge bases (i.e., drug–drug interactions or patient education materials) are made available on a *weekly* basis. Institutional drug buying practices, retail pharmacy services, and Pharmacy Benefit Manager functions have created the need for *daily* updates of drug pricing information.

First DataBank also has many international drug databases that were developed by a professional staff consisting of native language speakers who best understand how drugs are used in other countries. As the Internet and global travel make the world "a smaller place," these knowledge bases will become even more omnipresent and obligatory.

Experience is critical to develop and maintain a comprehensive database of drug information. First DataBank has been in this business for over 20 years, having spent virtually all of that time developing, maintaining, and enhancing the most comprehensive drug, medical, and nutrition knowledge bases in the world. Our knowledge bases have evolved along with new technologies in healthcare and continue to develop as the Internet and mobile devices become part of clinical practice. First DataBank offers customization for every client's file in terms of record format, formulary selection, media specifications, updates, and user-specific data elements. As

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a result, our customers save valuable programming and processing time.

DRUG KNOWLEDGE BASES AND THEIR CLINICAL MODULES

First DataBank creates and maintains some of the largest and most comprehensive drug and healthcare knowledge bases in the world, including NDDF Plus™, based on the industry standard National Drug Data File®. One of the industry's most trusted and widely used sources of up-to-date drug information, NDDF Plus combines descriptive and pricing data with a selection of advanced clinical support modules. NDDF Plus delivers information on every drug approved by the Food and Drug Administration (FDA). Clinical modules are available to support healthcare professionals in making critical decisions about dosing and orders, interactions, allergy alerts, disease contraindications, drug identification, and much more. Plus, several modules offer drug information specifically written for the consumer. NDDF Plus is used in a wide variety of applications, such as:

- Determining drug indications.
- Identifying potential contraindications.
- Helping prevent adverse drug events.
- Identifying drug–drug and drug–food interactions.
- Identifying potential drug interactions with alternative therapy agents.
- Offering printed patient education and counseling messages.
- Prioritizing medication warning labels for patients.
- Listing recommended doses for common drugs.
- Performing indication-specific dose range checking.
- Identifying undesired effects of drugs on lab tests.
- Supporting electronic medical records.
- Handling prescriber order entry.
- Analyzing drug pricing trends.
- Facilitating drug formulary management.
- Accelerating claims processing and adjudication.

First DataBank offers comprehensive international drug knowledge bases for several countries outside the United States, including Canada, Argentina, and Australia. First DataBank Europe, located in Exeter, England, develops drug knowledge base products for the United Kingdom.

Examples of clinical functionality in drug knowledge bases are described below for Patient Education, Drug Interactions, and Prescriber Order Entry modules. Many other pharmaceutical decision support modules are also available and include Drug/Disease Contraindications, Drug Indications, Pregnancy and Lactation Precautions, Geriatric/Pediatric Warnings, Minimum/Maximum Dose Checking, and Duplicate Therapy/Ingredient Checking. A few specific modules are highlighted.

Patient Education

Patient Education Monographs were written for consumers. They are both comprehensive and customizable, covering the most common prescription and OTC medications. The format of these patient education monographs is flexible and is available in English and Spanish. Other patient education materials are available including Prioritized Label Warnings that indicate which ancillary "stickers" should be placed on a medication being dispensed and Counseling Messages to be used as reminders for healthcare professionals.

Drug Interactions

First DataBank's drug interaction modules are meant to be able to detect all clinically significant drug–drug interactions for a given patient in either a prospective or retrospective manner. Drug–food interaction information is also available. Interactions are classified by severity, and documentation levels are also noted in coded fields for searching and filtering applications. Full text monographs describe the drug–drug interaction in detail and include reference citations in MEDLINE format. A "consumerized" version of the drug–drug interaction monograph has been created for systems that allow patients to monitor their medications.

Prescriber Order Entry

Prescriber Order Entry Module (POEM™) provides a database of the most common medication orders. These orders are specific to drug, route of administration, formulation, age, indication/use, and weight or body surface area, if applicable. This enables more accurate and efficient point-of-care computerized order entry applications to prevent errors at the prescribing stage of drug delivery.

INTEGRATED CONTENT SOFTWARE

Success in today's drug information marketplace requires products that can be developed quickly and economically, lowering the cost of entry into a given market. Toward that end, First DataBank offers a number of application

development toolkits that minimize lead times and make more efficient use of scarce resources.

Drug Information Framework™

The Drug Information Framework™ enables developers to build healthcare solutions faster, using the time-tested NDDF Plus knowledge base and critical decision-support modules. The Framework gives developers a choice of technologies and access layers, so it can adapt to most platforms, operating systems, development tools, and relational databases. Application environments can include the Internet; client/server networks; stand-alone desktops; and handheld wireless devices.

Drug Information Framework components encapsulate drug information in intuitive objects, which shortens the typical programmer learning curve and development cycle. These components simplify system implementation, resulting in quicker, easier deployment of systems offering point-of-care, patient-specific drug information, as well as convenient access to full-text clinical monographs.

AHFS Framework™

The AHFS Framework™ enables developers to easily embed drug content into pharmacy and clinical information systems. It can be used to rapidly integrate two respected drug knowledge bases: the American Hospital Formulary Service (AHFS) Drug Information® monographs, and First DataBank's NDDF Plus. Combined, they allow healthcare professionals to have seamless access to comprehensive drug information, within their usual workflow systems.

Rx InHand™

With Rx Inhand™, developers have a powerful tool for creating stand-alone handheld applications. This drug navigation and drug utilization review (DUR) engine enables developers to easily create systems for use by physicians to write prescriptions and to screen them on a handheld device for possible medication errors, thus potentially minimizing adverse medical events.

RxWeb™

RxWeb™ provides instant access to drug information, navigation capabilities, and clinical-screening functionality over the Internet. Using the latest Web browser technology, RxWeb enables the developer to offer proven drug screening (via NDDF Plus) with little or no development time. With RxWeb, software developers can create Web-based applications that provide information on over 100,000 marketed drugs, as well as alternative therapies.

REFERENCE PRODUCTS

First DataBank has developed numerous drug reference products for healthcare applications, in both print and electronic forms. Most of these products can be deployed on an individual desktop, a local area network and, in some cases, over the Internet or intranet.

AHFS*first*™

AHFS*first*™ combines into one easy-to-use package two of the most widely used sources of unbiased drug information—NDDF Plus and the AHFS Drug Information® monographs from the American Society of Health-System Pharmacists®. It links over 100,000 drugs from NDDF Plus to the AHFS monographs, providing maximum coverage from two respected sources. This sophisticated reference makes it possible, in just seconds, to find information on drug interactions, contraindications, adverse reactions, and precautions. The AHFS*first* Web edition brings this capability to users of the Internet or intranets. AHFS Drug Information monographs are also available as a data-only product.

Evaluations of Drug Interactions™

First DataBank's Evaluations of Drug Interactions™ (EDI) provides the most comprehensive printed source of drug–drug interaction information available. Containing interactions on both prescription and over-the-counter drugs, this two-volume loose-leaf textbook of drug monographs is the only source endorsed by the American Pharmaceutical Association.

SPECIALTY SOFTWARE

In addition to drug information products, First DataBank has developed several interactive software products intended for direct use by healthcare specialists, including nutritionists and physicians.

Nutritionist Pro™

Nutritionist Pro™ software represents the next generation of nutrition-analysis tools from First DataBank.

With the most comprehensive food knowledge base and set of program features, Nutritionist Pro provides thorough analysis of diets, recipes, and menus. The intuitive user interface design and powerful functionality of Nutritionist Pro can help ease the workload and boost the productivity of nutrition professionals in virtually any healthcare delivery, food service, or educational setting.

ANTICIPATING FUTURE NEEDS

In healthcare, we are today at a crossroads of yet, another of many notable technical developments. Personal computers have become ubiquitous and easier to use for healthcare professionals and patients. The newly available mobile or handheld devices have become more practical for real-time computing. Through the Internet or handeld device, there is ready access to a patient's medical information. With these tools, the art of practicing medicine is truly about to change. An electronic information resource for the Internet and for handheld devices, as for other platforms, requires that the data meet specific standards of reliability. First DataBank information is "tried and true," a tested, authoritative source of such information.

First DataBank has anticipated this wave of technological change in medicine and has developed an array of software and middleware for ease and effectiveness of decision support implementation for these platforms. Time-to-market has become an absolutely critical factor in the success of healthcare IT applications. The Internet, cost containment, IT undercapitalization, and a host of other factors impacting the healthcare industry have created a demand for the rapid deployment of new applications.

First DataBank is not only meeting healthcare challenges but is also leading the industry into an era of greater patient safety and knowledge.

FIRST DATABANK AS A HEARST CORPORATION SUBSIDIARY

The visionary behind First DataBank is founder and President, Joseph L. Hirschmann, Pharm.D. Doctor Hirschmann started the company after a distinguished academic career at University of California, San Francisco. Another of his accomplishments that lives on today is the *Textbook of Therapeutics: Disease and Drug Management*, which was previously known as *Clinical Pharmacy and Therapeutics*.

First DataBank became part of the Hearst Corporation in 1980. The Hearst Corporation is one of the world's largest diversified communications companies, with interests in newspapers, magazine, book and business publishing, television and radio broadcasting, cable network programming, and new media activities. First DataBank remains under established independent leadership, while benefiting from the support and financial stability offered by The Hearst Corporation.

LOCATIONS

The First DataBank home office is located in San Bruno, California, just a few miles from the San Francisco airport. The company also has offices in St. Louis, Missouri; Exeter, England; and Indianapolis, Indiana.

Formulary Systems

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INTRODUCTION

Formulary systems are an essential tool used in a variety of settings including hospitals, ambulatory clinics, health plans, pharmacy benefit management companies, and government agencies. This tool, if used correctly, promotes rational, clinically appropriate, safe, and cost-effective pharmaceutical care.

The term "formulary" has been used to describe a published list of medications used by an organization, from which prescribers can choose therapy for their patients. Historically, an "open" formulary implied that the list was fairly inclusive of any medications the prescribers wanted. A "closed" formulary was a finite list that reflected the clinical judgment of a group of physicians, pharmacists, and other health care professionals meeting regularly to choose the most appropriate drugs for the list. Most pharmacists have stopped using "open" and "closed" because few contemporary formularies are truly "open." A formulary now typically refers to a book or on-line publication used by the organization that contains the approved drug list and other prescribing information deemed useful by its editors.

A formulary system goes much beyond a publication or list of drugs. A coalition of national organizations representing health care professionals, government and business leaders has offered this definition:

> Drug Formulary System—an ongoing process whereby a health care organization, through its physicians, pharmacists, and other health care professionals, establishes policies on the use of drug products and therapies that are the most medically appropriate and cost-effective to best serve the health interests of a given population.[1]

This review of formulary systems covers their history, structure, positive and negative outcomes, and possible future directions.

HISTORY

Formularies were first developed in hospitals during the 1950s. The pharmaceutical market was experiencing unprecedented growth. For example, 17 different companies were marketing 45 different oral penicillin preparations.[2] Institutional policies were developed that allowed pharmacists to dispense a generically equivalent drug for a brand name product prescribed by physicians.

The pharmaceutical industry and physicians, represented by the National Pharmaceutical Council and the American Medical Association (AMA) respectively, successfully worked to get state laws passed forbidding this substitution by pharmacists. While community pharmacists complied, hospital pharmacists resisted. In the late 1950s, the American Society of Hospital Pharmacists (ASHP) published a set of minimal standards for pharmacies in hospitals with guidelines for their interpretation. Among the standards developed was a call for the implementation of a formulary system. Interestingly in 1959, the successful launch of another ASHP publication, the American Hospital Formulary Service, a reference book reviewing the key characteristics of drugs, greatly advanced ASHP's financial status and added to the organization's sphere of influence.[3]

By the 1960s, many hospitals were successful in developing institutional procedures that gave prior consent for physician authorized pharmacists to select generic alternatives under what was called a formulary system.[4] The American Hospital Association (AHA) and ASHP issued joint statements on the legal basis of a hospital formulary system and the guiding principles for operating it. A few years later, the AMA and APhA participated with AHA and ASHP to revise the guidelines to the mutual satisfaction of all parties in a way that would not alienate the pharmaceutical industry.

In 1965, two significant actions occurred that promoted formulary systems. Medicare administrators borrowed freely from ASHP's publications to create standards for institutional health care resulting in a Medicare bill listing the use of a formulary system among the eligibility requirements of Medicare reimbursement. Also, the Joint Commission required an active pharmacy and therapeutics (P&T) committee for hospital accreditation.

Even with these supporting documents and accreditation standards, adoption of formulary systems was not as fast as many anticipated. In the 1970s, two surveys revealed surprising results. In the first, of the 172

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Medicare-approved hospitals responding, 31 did not have a formulary system in place even though Medicare required one.[5] The second, looking at academic medical centers with 500 beds or more, found that the majority of formularies analyzed were simple drug lists and were not used to guide prescribing decisions.[6]

As the value of formulary systems became apparent, their acceptance grew, at first just in the hospital setting but later expanding to ambulatory sites. In 1986, the Pharmaceutical Manufacturers Association officially accepted the concept of therapeutic interchange for hospital inpatients, but opposed its use in other settings. The AMA released a policy on drug formularies and therapeutic interchange in both inpatient and ambulatory care settings in 1994.[7] This brought the AMA's views on formularies into close alignment with ASHP. In the most recent survey of pharmacy practice in acute care settings, more than 90% of health-systems had P&T committees responsible for formulary system development and management.[8] Pharmacy directors reported using pharmacoeconomic and therapeutic information in their system's formulary development process. Today, drug formulary systems are considered an essential tool used routinely by health plans, pharmacy benefit management companies, self-insured employers, and government agencies.

THE STRUCTURE OF FORMULARY SYSTEMS

The development of a formulary system within an organization rests with a multidisciplinary committee. In the hospital and health system setting, this is typically called the P&T committee. Virtually all hospitals and health-systems have a P&T committee.[8] P&T committees usually meet six to eight times annually. An ASHP Position Statement on formulary management declares that decisions should be based on clinical, quality of life, and pharmacoeconomic factors that result in optimal patient care.[9] It advises against decisions solely based on economic factors. The Position Statement also recommends that decisions must include active and direct involvement of physicians, pharmacists, and other appropriate health care providers. This may include dieticians, nurses, administrators and quality management coordinators.

Formulary system management falls into three general categories: drug selection for formulary inclusion, formulary maintenance, and medication use evaluation.

Drug Selection

Drug evaluation for inclusion on a formulary should involve a careful assessment of scientific evidence, in particular, peer-reviewed medical literature, including randomized clinical trials, pharmacoeconomic studies, and outcomes research data. If a drug is a new pharmacologic class, unlike any other available drug, the review will focus on efficacy, safety, and the potential value to the organization's patient population. For drug's that are additions to an existing pharmacologic class, the evaluation takes on a more comparative nature. Reviewers look for studies that compare the new agent to the agent currently listed on the formulary. If these are limited or unavailable, the comparisons are difficult and more subjective. If two agents appear similar in all clinical respects, the decision may be a financial one. This process often results in class review as described later. Reviewers must remember that new agents coming on the market have been tested in a limited number of patients. Because a drug's full adverse effect profile may not be evident when first released, many committees choose to stay with the older drug already listed on the formulary until sufficient information is published.

Two key components of formulary drug selection are generic substitution and therapeutic interchange. Generic substitution is the substitution of one drug product for another when the products contain the same active ingredients and are chemically identical in strength, concentration, dosage form, and route of administration. The formulary will list the drug by its generic name, strength, and dosage form. The product dispensed will be the least expensive one. As the price of products change, the product dispensed may change as well. When this occurs, the pharmacist should inform the patient if the physical appearance (e.g., color, tablet size) of their medication has changed. The patient should be assured that the new medication is identical to the previous one.

Therapeutic interchange is more complex that generic substitution. The AMA defines therapeutic interchange as the authorized exchange of therapeutic alternates in accordance with previously established and approved written guidelines or protocols within the formulary system.[7] Therapeutic alternates are drugs with different chemical structures but which are of the same pharmacologic and/or therapeutic class. They can be expected to have similar therapeutic effects and adverse reaction profiles when administered to patients in therapeutically equivalent doses. The AMA does not support therapeutic substitution defined as dispensing a therapeutic alternate for the product prescribed without prior authorization of the prescriber. Therapeutic interchange in institutional health systems has been used successfully for years. Working out an acceptable procedure for therapeutic interchange by the P&T Committee may be easier in this setting. Therapeutic interchange in outpatient drug programs in less structured ambulatory and managed

care settings may be more difficult and has been criticized.[10]

Formulary Maintenance

Maintaining a formulary is an ongoing process. Policies and procedures for requests to add and delete drugs from the formulary must be in place. This includes changing recommendations for therapeutic interchanges and components of drug use guidelines. As the medical evidence changes in the published literature, the formulary system must be able to quickly respond.

Therapeutic class reviews are an important part of formulary maintenance. The pharmacologic class of drugs selected for review should be prompted by criteria set by the P&T Committee.[11] These criteria may include the number of adverse drug reaction reports, new information in the medical literature, or drug class expenditures. Some groups may choose to review the class whenever a request is received to add a new drug from that class to the formulary. The goal is to always have the best agents within a class available based on the latest medical evidence. At the time of the review, new drug use or treatment guidelines may be considered.

The formulary system should include a mechanism for patients to receive a drug not listed on the formulary if it is truly needed. A review of these non-formulary drug requests may offer insight into areas where the formulary is not meeting the needs of the health system's patients. This is true if the review reveals that requests for a specific agent are justified and frequent. The review may show that education is needed for the prescriber to steer them toward a more rational formulary choice.

Medication Use Evaluation

Medication use evaluation (MUE) is a performance improvement method that is an important part of the formulary system. MUE focuses on evaluating and improving medication use processes with the goal of optimal patient outcomes.[12] It involves establishing criteria, guidelines, treatment protocols, and standards of care for specific drugs and drug classes and the medication use process (prescribing, preparing and dispensing, administering, and monitoring).

POSITIVE AND NEGATIVE OUTCOMES

The description of the formulary system leads one to believe that it would lead to positive outcomes. In the hospital setting, a significant association has been shown between decreased costs and a well-controlled formulary, therapeutic interchange, or both.[13] Hospitals that used either strategy spent 10.7% less for drugs than those that used neither. Hospitals using both spent 13.4% less than those that used neither. An estimated $100 million in pharmacy expenditures was saved by the Department of Veterans Affairs (VA) in two years by implementing a national formulary.[14] A committee of the Institute of Medicine found that for inpatient discharges for conditions likely to be affected by the VA formulary's limited drug list, no increases in hospitalizations were found.[15] The committee did recommend to increase physician representation on formulary committees and to abandon the requirement that a drug be marketed in the United States for a year before it could be admitted to the formulary. However, convincing research clearly documenting improved patient outcomes is scarce.

Managed care organizations have used formularies to rein in drug costs but a controversial study concluded that formularies produced an opposite effect.[16] Researchers found that restrictions on drug availability were linked to increases in other services shifting costs by increasing the use of either nonrestricted drugs or other health care services. This study included the use of the restriction method called prior authorization, a method used to discourage the routine use of an expensive drug by requiring an approval process before the agent could be prescribed. In general, the results showed that the more restrictive the formulary, the higher the drug costs and the higher the number of prescriptions, outpatient and emergency room visits, and hospitalizations per patient per year. The study design and conclusions have been highly criticized.[17]

A prior authorization technique involving non-steroidal anti-inflammatory drugs (NSAIDs) in Medicaid patients was shown to be highly effective.[18] NSAIDs not available generically were place on prior approval status. This lead to the increased use of generically available NSAIDs as first line therapy. For a two-year period, the result was a 53 percent decrease in expenditures ($12.8 million) with no concomitant increase in Medicaid expenditures for other medical care.

ETHICAL ISSUES

Few ethical questions have been raised in the hospital setting but in the outpatient setting, there may be concerns. Health plans may try to manage pharmacy costs by offering incentives to physicians for prescribing lower cost drugs. This may be depicted as unethical because the strategy appears to be purely cost driven and possibly

lowering the quality of care. However, such incentives may improve quality. For example rewarding physicians for following recent guidelines for treating hypertension (an inexpensive beta-blocker and a generic thiazide).[19] In presentation at the Joseph A. Oddis Colloquium on Ethics, it was suggested that the pharmacist play the role of a pharmacoethicist on P&T Committees.[20]

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