

The Economics of Prescription Drug Pricing
Background Paper

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A complex mix of government regulation and market competition characterizes the economics of prescription drug pricing. This paper provides background information necessary to understand this dynamic and evaluate potential change. It examines prescription drug price trends over time. Increasing growth is attributed to development and marketing of new products and the increasing volume of drugs prescribed. The growing number of people with prescription drug insurance coverage also increases demand and price as does growth in direct-to-consumer advertising. Drug price inflation is less of a factor. Pricing is strongly affected by patent law and the regulatory structure that partially determines the time and cost to bring a new drug to market. The industry pricing and cost structure is examined with a focus on how potential changes in pricing might impact future investment in research and development, and innovation.

Next, the paper describes cost control strategies in certain organizations such as pharmacy benefit management organizations (PBMs), managed care organizations, the Medicaid program, and other government purchasers (VA, federal employees). A number of strategies are examined that have been tried or proposed to control costs including: increased cost sharing for consumers, formularies, discounts and rebates, reference pricing, the greater use of generics, and disease management. The final section examines international comparisons and re-importation strategies.

I. INTRODUCTION

The pharmaceutical market is neither fully regulated nor completely subject to the free market. The mix of government regulation and competition is complex and has shifted over time. Developers and manufacturers of drugs are protected by patents and have a monopoly on production for a set period of time. Some level of protection is essential to encourage private sector investment in research and development. Drugs must meet certain standards for safety and efficacy and must undergo a rigorous and time-consuming process to gain initial approval by the Food and Drug Administration. The National Institutes of Health provides considerable funding for basic research and drug development. Government subsidies are available to certain purchasers, which increases access to and demand for pharmaceuticals (Medicaid provides free or low cost drugs to many poor Americans, and the cost of drug coverage provided by an employer is excluded from taxation). A new Medicare drug benefit for senior citizens is probable in the near future, and will likely increase the government's role in the market as a purchaser and a regulator.

Competition is taking place within and around this regulatory framework. Pharmaceutical companies have far greater ability to set price in the United States than in other industrialized nations. Organized purchasers, including government purchasers have some ability to negotiate price concessions in the marketplace. This system results in lower prices for some but may increase prices for others. We know that different purchasers pay different prices for prescription drugs. The uninsured, or those unaffiliated with group purchasers, generally pay the highest prices and this limits their relative ability to purchase prescription drugs.

Some drugs are essential to life. They prevent heart attacks, stop strokes, or enable asthmatics to breathe. Other drugs enhance life. Reduction of dermatological blemish is a beneficial side effect of a particular contraceptive, anti-fungal medicine improves ones' look in sandals, and products abound to slim one's figure and restore one's hair. As a society, we have to decide who has access to these drugs. Should the market determine distribution under current regulations? Should government provide additional subsidies and if so, to whom and for what? Creating new drug benefits will increase access to drugs and lead to increased utilization and costs. Should these costs be controlled, and how? What impact will this have on the market? If we choose to regulate price by limiting manufacturer monopolies (patent life), will this stifle research and development? Can subsidies and competition be structured in a way to promote continued innovation? This paper provides information necessary to consider these questions and identifies new approaches to regulation and competition. It examines factors responsible for cost increases, changes in patent law, strategies of organizations that have attempted to control costs, and different pricing in international markets.

II. DRUG COST TRENDS

Health expenditures have grown more rapidly for prescription drugs than for any other type of medical care. According to the Health Care Financing Administration (HCFA), total costs for prescription drugs increased 79 percent from 1993 to 1998, an average of 12.4 percent per year (HCFA, 2000). During this period drug expenditures climbed from 5.6 percent of total health care spending to 7.9 percent. Berndt, using Department of Labor statistics, reports a 12.8 average annual growth rate between 1994 and 1999 (Berndt 2001). Additional studies confirm this upward trend (Express Scripts 1999).

Although, these numbers are large, and the trend is significantly upward, uncertainty remains about the value of increased costs relative to clinical benefits. Uwe Reinhardt points out that drug expenditures account for just 1.3 percent of the gross domestic product -- less than Americans spend annually on alcohol and tobacco, and far less than for entertainment (fees and admissions only) (Reinhardt 2000). Limited information exists about the societal benefit of these expenditures (Newmann, Sandberg et. al.). What gains are achieved in terms of quality of life from these expenditures? How do these costs impact total health care system costs? These calculations are difficult to do in the aggregate; the research we do have is the result of analyzing one drug at a time.

The cost of prescription drugs, as well as utilization varies considerably among individuals. Increased insurance coverage and lower out of pocket costs have shielded many from the effects of higher drug costs, but some groups (the uninsured, senior citizens, and people who need a disproportionately high number of drugs) have significant access problems. Private drug insurance coverage and government programs, which paid for only 4 percent of drug costs in 1960, accounted for 74 percent in 1998. Corresponding out-of-pocket costs decreased from 96 percent in 1960 to 26 percent in 1998. However, particular individuals have experienced considerable out of pocket cost increases. In some cases, limited resources force some to choose between prescriptions and other essentials, or result in patients taking less than their prescribed dose.

With a few exceptions, Medicare does not cover outpatient prescription drugs. Older Americans (those over 65) spend almost three times as much of their income on health care (21 percent) than the rest of the population (8 percent) (Committee on Government Reform, 1999). Thirty five percent of seniors do not have prescription drug coverage, and many with coverage have high deductibles and caps on total dollar coverage. The 3 (out of 10) standardized Medigap policies (supplemental Medicare policies) that offer prescription drug coverage are very expensive. Two of these policies have a \$250 deductible, 50 percent copayment for each drug, and an annual cap of \$1,250. The other plan has the same level deductible and copayment with a higher cap of \$3,000 (Families U.S.A, 1999).

High use seniors are disproportionately impacted by higher drug prices. While the average annual out of pocket cost seniors pay for drugs is \$200, 29 percent pay more than \$500, 14 percent spend more than \$1,000 and 4 percent more than \$2000 (Gluck 2000). This concentration of expenditures indicates why a number of legislative proposals include some form of catastrophic protection in formulating a Medicare drug benefit. Expanded insurance coverage for seniors would increase access and utilization. First dollar coverage increases access the most, but removes the consumer from the cost effects of utilization (moral hazard) and could lead to inefficiencies. (For example, using higher price drugs when equally effective lower cost alternatives are available, or using drugs when costs exceed benefits.) Government actions to increase access to seniors and other high end users must be balanced with concerns of efficiency and cost containment.

A. Factors Contributing to Growth

The development of new products, increased utilization, and inflation (price increases for existing products) all influence total costs. Studies indicate that the most important factors are the development of new drugs and the characteristics and volume of drugs prescribed. There are two types of drug innovation: those designed to treat conditions not previously treated by pharmaceuticals, and those that improve current pharmaceutical treatments. Drugs that represent significant breakthroughs or new treatments are generally priced high, while new drugs that have close substitutes are priced more competitively. Pharmaceutical growth is pushed by an expanding supply of new products and direct-to-consumer advertising and pulled by increased consumer

demand, because of increased insurance coverage, rising personal income, and an aging population.

1. Inflation

Price inflation is not the most significant factor accounting for recent increases in total pharmaceutical spending. Using cost per daily dose as a measure of price, Dubois et. al. (2000) found that price was responsible for between 7 and 29 percent of increased costs per year. Berndt reports that about 20 percent of the average annual growth rate between 1994 and 1999 can be attributed to price increases (Berndt 2001). The Brandeis Schneider Institute for Health Policy study (2000) found that when controlling for increased use, days used, and strength of dosage, about 5 percent of the annual increase is attributable only to price.¹

Table 1, Consumer and Producer Price Indices for Prescriptions Drug Products, provides a description of health care inflation data for the 1990s. It shows that prescription drug inflation was high in the early 1990s, in line with other health care services. However, in the later half of the decade prescription drug inflation moderated significantly.

¹ The Brandeis study found that the annual rate of growth for the most common drugs was 20.3 percent between 1996 – 1999 (.9% price, 3.5% drug mix, 3.9 percent days on medication, 7.8% prescriptions per user, 2.8% number of users, 1.4% interactions).

Table 1.
Consumer and Producer Price Indices for Prescription Pharmaceutical Products

Year	Physicians Services*	Hospital and Related Services*	Prescriptions Drugs*	Prescription Pharmaceutical Preparations**
1990	7.1%	10.9%	10.0%	8.9%
1991	6.0%	10.2%	9.9%	8.3%
1992	6.3%	9.1%	7.5%	7.1%
1993	5.6%	8.4%	3.9%	4.5%
1994	4.4%	5.9%	3.4%	2.5%
1995	4.5%	5.0%	1.9%	3.1%
1996	3.6%	4.5%	3.4%	3.2%
1997	3.0%	3.3%	2.6%	3.1%
1998	3.0%	3.3%	3.7%	3.9% ^a
1999 ^b	2.8%	4.2%	5.7%	3.8%

Source: U.S. Bureau of Labor Statistics, Table first reported in briefing paper for the Seventh Princeton Conference, Access to Pharmaceuticals, Council on the Economic Impact of Health System Change, May 11, 2000.

*Based on the Consumer Price Index (CPI)

**Based on the Producer Price Index (PPI)

^a The PPI data for prescription drugs contain several extreme outliers for the early months of 1998. Index values for February and March were imputed based on the average monthly percentage increase for the other months in 1998.

^b The data for 1999 are preliminary

2. *New Drugs*

New products are a major source of pharmaceutical cost increases. Technological advances, scientific breakthroughs, and the result of huge investments in research and development led to a plethora of new medications (protease inhibitors for HIV infection,

human growth hormone, Viagra, third and fourth generation anti-depressants, beta blockers, blood thinners, etc. etc). Brendt (2001) reports that since 1997 about 46 percent of expenditure growth can be attributed to new products. A study by the Barents Group (1999) found that drugs introduced since 1992 account for 65 percent of overall expenditure growth from 1993 to 1998. Merlis (2000) concludes that the cost of drugs introduced in the last half of the 1990s were about two and a half times more expensive than existing drugs.

The number of new drugs or new molecular entities (NMEs) approved by the Food and Drug Administration (FDA) has grown enormously over the past decade. From 1987 through 1993, FDA approved an average of 24 NMEs per year. From 1994 through 1999 the agency-approved rate jumped nearly 50 percent to 35.5 NMEs per year (Berndt 2001). ExpressScripts, a pharmacy benefits manager (PBM), reported that nearly half the growth in enrollee expenditures from 1994 to 1998 was due to the cost of drugs introduced since 1994 (ExpressScripts, 1999). Direct-to-consumer advertising appears to have a significant impact on new drug utilization.

DeMasi concluded that some new drugs are offered at a discount and others at a premium depending on whether a close substitute is available and what the perceived value of the drug is to the patient and the physician (DiMasi 2000). If the FDA gives a drug a high rating based on having significant benefits over existing therapies, price is generally set higher. DeMasi's data also showed little impact from pure price inflation above that of the general economy.

3. Utilization

The number of people receiving prescription drugs is increasing as is total prescriptions per person. Merlis reports that the introduction of new drugs contributed heavily to utilization growth (Merlis 2000). “About half the spending increase attributable to new drugs was due to utilization, about half due to the fact that they were more expensive” (Merlis 2000). Once again there are significant variations by drug type. Brandeis and Merck-Medco used cost per day as a measure of volume and came to similar conclusions. Brandeis attributed 60.7 percent of annual growth to increased utilization. Merck-Medco attributed 64.0 percent. While the numbers vary, it is clear that total prescription drug spending is being pushed by the increased utilization, particularly of new, often more expensive, drugs.

4. Insurance

Insurance coverage increased significantly since the 1960s and dramatically in the past decade. The seminal Rand study in the 1980s demonstrated that prescription drug use increased substantially for people with a drug insurance benefit. As coinsurance fell from 95 percent to 25 percent, drug expenditures increased by 33 percent (Brandt 2001). The proportion of pharmaceutical costs paid by insurance has increased from 3.5 percent in 1965 (92.6 percent of costs were paid out-of-pocket), to 20 percent in 1980 (66 percent paid out-of-pocket), to 46.8 percent in 1995 (33.9 percent out-of-pocket). Over this time,

Medicaid also picked up an increased share of prescription drug costs and has become the largest single purchaser of prescription drugs. In 1995, Medicaid provided drug coverage to 15.8 percent of Americans. By 1998, seventy percent of the population had some type of prescription drug coverage (Brandt 2001). However, for a concentrated minority of people with high drug expenditures (particularly the elderly), insurance may be unavailable or inadequate.

5. Direct-to-consumer advertisement

Since the FDA relaxed advertising regulations in 1997, Americans' exposure to direct-to-consumer drug advertising moved from a rarity to a near daily experience. The pharmaceutical industry spent \$905 million dollars in advertising in the first half of 1999, a 43 percent increase from the year before (Wilkes, Bell et. al. 2000). Survey analysis in Table 2, Consumer Response to Direct Drug Marketing, indicate that these ads influence consumer behavior. In total, 56 percent of the people who saw an ad reported reading it carefully, 35 percent asked the doctor for more information, 19 percent actually asked for the drug, 17 percent clipped the ad and 9 percent called the drug company for further information. People generally found educational value in the ads. Physicians, on the other hand, complain that these ads reduce their autonomy. A Barents study (1999) showed that the four fastest growing categories of drugs included 7 drugs that had the most direct-to-consumer advertising spending in 1998. Combined, these studies make a compelling case that direct-to-consumer advertising can successfully push demand.

Table 2
Consumer Response to Direct Drug Marketing

Consumer response	Percent of people who saw ad
Read ad carefully	56 percent
Asked doctor for more information	35 percent
Asked for the drug	19 percent
Clipped the ad	17 percent
Called the drug company for info.	9 percent

Source: Wilkes, Bell et. al. 2000

Table 3, Prescription Drugs with the Most Direct-to-Consumer Advertising 1998, list the top 12 drugs with the highest advertising budgets and their ranking based upon total prescriptions dispensed. Seven of the 12 highest advertised drugs are also among the top 50 drugs sold.

Table 3.
Prescription Drugs with the Most Direct-to-Consumer Advertising 1998

Drug	Indication	Direct-to-consumer advertising (\$ millions)	Top 200 Ranking
Claritin	Antihistamine	\$150.2	11
Propecia	Hair loss	\$91.0	200+
Zyrtec	Antihistamine	\$75.2	48
Pravachol	Cholesterol-lowering	\$59.6	29
Zyban	Smoking cessation	\$54.6	200+
Allegra	Antihistamine	\$52.5	59
Prilosec	Anti-ulcer	\$49.7	5
Zocor	Cholesterol-lowering	\$41.6	15
Evista	Osteoporosis	\$38.9	200+
Prozac	Anti-depressant	\$37.5	8
Premarin	Hormone replacement	\$37.0	1
Imitrex	Migraine	\$36.4	79

Source: Prescriptions Drug Trends – A Chartbook, The Kaiser Family Foundation, July 2000 p. 47.

III. PATENT PROTECTION

Pharmaceutical manufacturers are given a monopoly on production for a patent protection period. Without this protection companies would not risk the millions of dollars necessary to bring innovative drugs to market. Longer FDA approval times and

increase testing requirements have shortened the actual monopoly time, some of which was restored by the Hatch-Waxman Act of 1984. This section examines the cost of bringing a drug to market, the patent process, and the changes in the regulatory structure over time.

The average drug takes 12 years to bring to market at an average cost of \$270 million (Mullins, Palumbo et. al. 2000). Grabowski and Vernon (2000) place the average cost at \$231 million. “The average success rate for compounds entering clinical testing was only 22 percent (Grabowski and Vernon 2000).” For every drug approved by the FDA, thousands of others are considered unsafe or clinically ineffective. Mullins and Palumbo (2000) identify three a three-phase approval process for new prescription drugs.

1. The first stage is to conduct pre-clinical development including animal testing for safety and biological activity. 70 percent of potential new drugs that make it through this phase are approved for the second stage of the process.
2. The second stage is to file an investigational new drug application with the FDA and to seek approval for clinical studies. 33 percent of the remaining drugs make it through this phase.
3. The third stage is clinical testing. 27 percent of the remaining drugs make it through this phase (Mullins, Palumbo et. al).

Patent protection encourages manufacturers to assume the risk associated with bringing a new drug to market. Once the drug is approved, the marginal cost of manufacturing is very small. The value is in the knowledge gained from the research and development, and that is protected by the patent.

Debate continues over the optimal amount of time drugs should be protected from competition. Shorter patent protection periods enable generics to enter the market more quickly, increase competition, and reduce prices. On the other hand, such a policy would reduce profits or potential profits and could discourage innovation and the development of new drugs. Ideally, patent time should be set at the period of time just necessary to cover research and development cost including an average return on capital for investments with a similar risk profile. But this differs by individual drug and is nearly impossible to predict.

A major policy controversy is whether or not the period of patent exclusivity provides industry with sufficient resources to cover research and development cost and to earn a reasonable return on capital. Grabowski and Vernon, using data from DiMasi, estimate an average breakeven exclusivity period of just over 16 years from the point of drug development. The average patent protection period is now estimated at 12 years. However, certain breakthrough drugs can and do yield large profits in shorter periods. This makes assessing the adequacy of the patent protection period difficult to determine.

In 1962, the **Kefauver-Harris amendments** created the Food Drug and Cosmetic Act, which stipulated that drugs must demonstrate evidence of efficacy. FDA approval time for new drugs increased from 1963 to 1996 as the approval process and clinical trials became more complex and numerous (Grabowski, Vernon 2000). In the early 1980s, generics had to duplicate much of the same procedures as new drugs. This

increased the protection period of the original drugs, but slowed down cost-saving alternatives.

The **Hatch-Waxman Act** in 1984 lowered barriers to generics, but at the same time increased the effective patent protection for new drugs that was caused by the approval process. Generics that could demonstrate bio-equivalence in the pre-patent period, were exempt from lengthy FDA approval requirements and thus could be brought to market more quickly. Hatch-Waxman recognized the fact that the 17-year patent protection was being eaten away by the increasing amount of time it took drugs to go through clinical trials and the application process. Hatch-Waxman increased patent protection by the sum of the FDA review time plus one-half of the clinical testing time capped at five years. This was also constrained to extend maximum effective patent life to 14 years. The law's effect was to increase the exclusive patent protection period by an average of 2.33 years to 11.7 years of exclusivity between 1990 and 1995 (Grabowski, Vernon 2000).

The General Agreement on Tariffs and Trade (GATT) Uruguay Round Agreement Act of 1994 increased the patent protection from 17 to 20 years. Grabowski and Vernon's analysis reveals that GATT provided little if any additional patent protection over Hatch-Waxman. Accounting for differences in the start date of patent protection and Hatch-Waxman regulatory and trial period offsets, GATT initially increased patent life modestly, but may actually shorten it for future drugs. GATT added

.40 years over Hatch-Waxman in the short term, but when fully implemented it may reduce protection time by an estimated .34 year (Grabowski, Vernon 2000).

IV. INDUSTRY PRICING STRUCTURE

In Congressional hearings and the media, the pharmaceutical industry has been accused of making excessive profits. Hearings examined higher prices paid by people without drug coverage, and international comparisons showing American prescriptions sometimes costing 4 or 5 times more than in other nations. This section briefly examines some of the literature on how rate of return is calculated and how prices are set.

Rates of returns on investments for pharmaceutical companies in 1997 ranged from 14.4 percent for Pfizer to 21.9 percent for Johnson and Johnson (average 18 percent). Advocacy groups claim this is excessive. The industry claims that these numbers are overstated. Rate of return is a ratio of after-tax operating income to the depreciated book value of assets. Since a large portion of the drug industry assets are in research and development (not more tangible assets like physical plant or equipment), the denominator does not take these costs fully into consideration. This inflates estimates of rates of return (Brealy Myers 2000). Brealy and Myers show that if research and development spending was accounted for in the same manner as capital expenditures, the rate of return on investments for the pharmaceutical industry would be considerably less.

Lu and Comanor (1998) examined the strategic pricing of new pharmaceuticals and found that price strategies vary by the type of innovation and whether the drug treats acute or chronic conditions. Prices for new drugs that are highly innovative and represent important therapeutic advances are typically set high and decline over time. Drugs that are substitutes are generally set at lower price levels to capture market share and often increase in price over time. Acute drugs tend to have higher prices than chronic drugs, controlling for the level of therapeutic advancement. This study attributes the bulk of higher pharmaceutical prices to more effective and innovative products. DiMasi (2000) reports similar findings, concluding that many, but not all, new classes of drugs tend to be offered at a premium. New drugs in an existing class tend to be offered at a discount. There is price sensitivity in the market, and the perception of product value to physicians and patients also influences price.

Drug prices vary widely by purchaser. Cook (2000) found that hospitals pay nine percent less than retail and HMOs pay 20 percent less. Discounts are based on volume and purchasers' ability to influence market share. Cook concludes that price sensitivity across purchasers, and high research and development costs coupled with low production costs, lead to a wide range of prices for similar products. This holds domestically and internationally. The uninsured, unaffiliated, and ungrouped tend to pay more. The industry offers rebates and discounts to high volume purchasers that can steer physicians and patients toward particular drugs. Price discounts are not given for drugs when substitutes are available, and they are not available for generics or new brand name drugs.

A Congressional investigation found that senior citizens without prescription drug coverage pay far more for their prescriptions than larger purchasers such as HMOs or the federal government. These seniors pay prices that can be up to six times greater. These price differentials were attributed to manufacturers, not retail pharmacies. An examination of the five drugs with the highest sales to seniors showed individuals pay 134 percent more than most favored customers (Committee on Government Reform, 1999). Detailed cost and differentials for these drugs are shown in Table 3, Average Prices for the Five Best-Selling Drugs for Older Americans Compared to the Price Paid by the Most Favored Customers.

**Table 3:
Average Prices for the Five Best-Selling Drugs for Older Americans Compared to the Price Paid by the Most Favored Customers.**

Drug/use (dose)	Price for Favored Customers	Average Price for Seniors	Average Differential for Seniors
Zocor/cholesterol (5 mg, 60 tablets)	\$27.00	\$107.66	\$80.66 (299 %)
Norvasc/high blood pressure (5 mg, 90 tab)	\$59.71	\$118.96	\$59.25 (99%)
Prilosec/ulcers (20 mg 30 caps.)	\$59.10	\$117.56	\$58.46 (99%)
Procardia XL/heart (30 mg 100 tab.)	\$68.35	\$133.22	\$64.87 (95%)
Zoloft/depression (50 mg, 100 tab.)	\$125.73	\$223.61	\$97.88 (78%)

Source: Minority staff, Special Investigations Division, Committee on Government Reform, Prescription Drug Pricing in the United States: Drug Companies Profit at the Expense of Older Americans, November 9, 1999.

There is considerable debate about the ability of drug manufacturers to segment domestic and international markets. Some argue that segmentation is economically efficient and allows manufacturers to increase revenue and contribute to fixed costs. Others maintain that drug companies abuse their monopoly power and derive excess profits. Further, they contend that different price levels may have little relation to the clinical benefits derived. Poor countries can generally purchase drugs at a relatively lower cost, but American seniors and those without drug coverage often pay the highest price for prescription drugs.

V. ORGANIZATIONAL EFFORTS TO CONTROL COST

This section examines three entities or organizations and their efforts to control prescription drug costs: PBMs and managed care organizations, Medicaid, and other federal programs. Details regarding cost control strategies are provided in Section VI.

A. Pharmacy benefit managers (PBMs) and managed care organizations (MCOs)

Pharmacy benefit managers started in the 1970s with the limited responsibility of paying drug claims, tracking cost-sharing requirements, collecting data, and preparing reports. With the onset of managed care and first dollar drug coverage, the role of PBMs expanded to managing costs and utilization. Five of the largest pharmacies in the United States own PBMs. HMOs directly managed the benefit for an additional 40 million, generally using the same techniques (Sanders 1997).

In 1998, there were 76 PBMs but less than a handful of firms dominated the field (Huskamp, Rosenthal et. al. 2000). In 1999, the top 20 PBMs managed 71 percent of prescription drugs at retail pharmacies covered by insurance. The top 3 firms (Merck-Medco, PCS Health Systems, and Express Scripts) control 45 percent of all prescriptions paid by third party payers (Mathematica 2000). By 1998, PBM services were being provided to 70 percent of people with drug coverage, some 200 million people. PBMs seek to control costs by managing drug utilization and negotiating price concessions from manufacturers and pharmacies. Huskamp et. al. (2000), while noting a dearth of evidence on cost effectiveness, identified two studies showing substantial savings. GAO in a study of three PBMs found between 20 and 27 percent savings (GAO, 1997). Grabowski and Mullins (1997) found between 14 and 31 percent savings.

A Kaiser Family Foundation report identified four primary strategies employed by PBMs to control costs: price discounts, particularly from pharmacies; price rebates from manufacturers; the use of formularies, including many with tiered copayments; and utilization management (Cook 2000). Table 1: Effectiveness of PBM management techniques summarizes the cost savings attributed to each of these strategies. Total cost savings were estimated at between 21 and 37 percent (see Table 4. Effectiveness of PBM management techniques). The majority of savings come from price reductions: discounts from pharmacies (13-15 percent), and rebates from manufacturers (2-6 percent). The use of formularies, including generic substitution, accounts for between three and nine

percent of savings. Utilization management accounts for between three and seven percent of savings. These cost savings techniques are described in detail below.

Table 4.
Effectiveness of PBM management techniques

PBM Technique	Percent Cost reduction
Price reductions	
Discounts from Pharmacies	13 – 15 percent
Rebates from Manufacturers	2 – 6 percent
Formularies and other therapeutic interventions including generic substitution	3 – 9 percent
Utilization management: prospective, concurrent and retrospective review	3 – 7 percent
Total Savings	21 – 37 percent

Source: Mathematica Policy Research Institute 2000; reported in Princeton Conference on Access to Pharmaceuticals briefing paper May 11, 2000. Table first reported in briefing paper for the Seventh Princeton Conference, Access to Pharmaceuticals, Council on the Economic Impact of Health System Change, May 11, 2000.

B. Medicaid

Medicaid is the single largest purchaser of prescription drugs in the country, covering 11 percent of Americans in 1996 (Kaiser 2000). Although each state has its own Medicaid program, and utilizes benefit management techniques, they still rely on federal provisions to control costs and insure access to a wide range of drugs. Medicaid provides prescription drug coverage primarily to low income individuals, families, and people with disabilities. Drug coverage accounted for only .8 percent of total Medicaid

costs in 1975, but rose to almost 9 percent by 1996 (\$10.7 billion) (Health Care Financing Review 1998). Medicaid payments for prescription drugs more than tripled in the 1990s (\$5.4 billion in 1991 to \$17 billion in 1999) (GAO 2000). All states provide Medicaid drug benefits. Manufacturers must sign rebate agreements in order to have their drugs available in this market.

The Omnibus Budget Reconciliation Acts (OBRA) of 1990 and of 1993 established national pricing criteria for Medicaid. States pay the same price that pharmacies pay wholesalers, plus a dispensing fee and minus a manufacturer's rebate. OBRA 1990 required drug manufacturers to give rebates to state Medicaid programs. The rebate for brand name drugs must equal 15.1 percent of the average manufacturer's price (AMP) or 100 percent of the difference between the average manufacturer's price and the lowest price they offer to their best customers (GAO 2000). The rebate for generics is equal to 11 percent of the AMP. The law also includes increased rebates if the price of a drug rises faster than inflation. Total rebates grew from \$553 million in 1991 to \$3.3 billion in 1999.

Medicaid rebates, like any piecemeal cost containment strategy, have repercussions in other parts of the market. GAO (2000) reports that evidence from the Medicaid rebates program suggests manufacturers adjust by increasing prices to other payers.

C. Other Government Purchasers

The Federal Supply Schedule (FSS), administered by the Veterans Administration, is a list of available drugs and their prices available to federal departments and agencies. The FSS contains over 17,000 products and prices. Manufacturers must list their drugs on the FSS in order to make them eligible for Medicaid reimbursement. The price is intended to equal or better the price manufacturers give to their most favored customers. The FSS price must, at a minimum, be 24 percent less than the non-federal average manufacturer price. This price must be available to the Veterans Administration, the Department of Defense, the Public Health Service (Indian affairs and certain community health providers), and the Coast Guard.

The VA also has a formulary that limits the number of drugs in four therapeutic drug classes. Only one or two drugs in each category are admitted to the formulary based on negotiations with manufacturers. Drug companies have been willing to reduce the price of particular drugs in order to be listed on the formulary. Contracts based on competitive bidding resulted in prices one-third lower than the corresponding FSS prices. The VA's capacity to control access to a formulary and its resulting ability to steer volume to a particular drug in a therapeutic class resulted in its receiving the largest discounts from drug manufacturers.

VI. COST CONTAINMENT STRATEGIES

With increasing drug prices and the possibility of a Medicare drug benefit that would increase demand and costs, a number of cost control strategies have been discussed. These include: cost sharing (deductibles, copayments, and coinsurance), formularies (list of reimbursable drugs), rebates and discounts, reference pricing, use of generics, disease management and utilization review, and re-importation of drugs from foreign countries.

A. Cost Sharing

Cost sharing includes copayments (generally a small amount paid at the point of purchase), coinsurance (the consumer pays a percentage of total costs, e.g., 20 percent), and deductibles (an amount paid before insurance kicks in). Kreling's (2000) review of the prescription drug copayment literature found that copayments limit the number of drugs used and temper total prescription expenditures. Studies show that raising copayments from \$3 to \$5 is associated with a five-percent reduction in the number of prescriptions. However, studies also show that even small copayments can stop lower-income people from purchasing essential medication (Soumerai et. al. 1994, reported in Maclure et. al 2001).

Many insurance companies and managed care organizations have switched from a single tier to a system of tiered copayments. For example, in 1996 Cigna charged \$5 for

each prescription before switching to a typical tiered copayment system described below (Kleinke, 2000).

1. Lowest copayment for generic drugs (\$5 and \$10)
2. Higher copayment for brand name drugs on the formulary (\$15 and \$20)
3. Highest copayment for brand name drugs not on the formulary (\$34 to \$40)

Three-tier copayment systems have been reported to save between six and 15 percent in prescription drug costs (Kreling, citing Segedin 1999). These savings are generally realized by health plans or plan sponsors. From two to five percent of these savings come from a switch to lower cost drugs and between four and 15 percent are attributed to savings from increased copayments. A tiered system still provides choice while making patients and physicians more aware of price. Tiers could also be structured to promote a more economically efficient outcome. For example, drugs that prevent high cost surgery or emergency room visits could be placed in the lowest tier or even provided without copayment. Drugs that enhance quality of life, like Viagra or Sporanox (to control toenail fungus), could be placed in the highest tier, or require full consumer payment.

Coinsurance requires the consumer to pay a fixed percentage of each drug purchased. Only 30 percent of plans require coinsurance compared with 80 percent that require copayments. The average coinsurance is 20 percent, but no research could be found on the cost effectiveness of this strategy (Kreling, 2000).

Catastrophic insurance plans with high deductibles make consumers the most conscious of price and limits what economists call moral hazard. Moral hazard occurs when one consumes more than one would otherwise because the out-of-pocket cost is

zero or greatly reduced. Eliminating deductibles and providing first-dollar insurance coverage makes prescriptions seem free and makes consumers the least conscious of cost. This drives up use and total expenditures.

B. Formularies

A formulary is a list of covered or reimbursable drugs. Formularies were originally designed to improve prescribing and drug use quality, but have increasingly been used as a part of cost control strategies. Formularies can be open and include all available drugs or closed with various levels of restriction. Tightly restricted formularies limit coverage to one or two drugs in a therapeutic class. The ability to steer patients to these particular drugs enables benefit managers to negotiate discounts with manufacturers. Eighty percent of employers who use pharmacy benefit managers (PBMs) have open formularies (Kleinke 2000). Preferred or partial formularies list drugs that have lower consumer copayments. Drugs that are purchased off-formulary are more expensive or are not covered at all. Three-fourths of HMOs have preferred or closed formularies, and they are becoming increasingly widespread (Kleinke 2000).

The research on formulary cost savings is largely inconclusive, partially because it is difficult to separate the effects of cost sharing and rebates associated with formularies. However, the experience of the VA and the increasing popularity of closed formularies for PBMs and HMOs are strong indications that limiting drug access by steering volume towards particular drugs within a therapeutic class can achieve

significant cost savings for particular groups. The impact of formularies on total drug expenditures across groups remains uncertain.

C. Rebates and Discounts

PBMs, HMOs, or other larger purchasers can often negotiate volume discounts with large pharmacies. This is usually negotiated as a reduction from the average wholesale price (AWP) and the payment of a dispensing fee. Purchasers have the leverage of eliminating a pharmacy as an option for their members, or encouraging members to use particular pharmacies. A 1996 Health Care Financing Administration funded study found PBMs were able to save between 10 and 15 percent off of the AWP. They typically charge dispensing fees in the range of \$1.95 to \$4.00 per prescription (Kreling 2000).

Manufacturers offer rebates to larger purchasers who can move market share towards a particular drug. Closed formularies give large purchasers leverage to negotiate manufacturer rebates. The greater the ability to shift market share to a particular drug, the greater the discount. Rebates are generally not given for new innovative drugs that do not have close substitutes. Rebates are not usually given for generic drugs, the price of which is most often initially set low to obtain market share. The Medicaid program's system of rebates described above is the most significant. PBMs generally receive rebates averaging \$1.00 a claim or five percent of drug spending (Wyeth 1999 reported by Kreling 2000).

D. Reference of Incentive Pricing

Incentive pricing is a system in which drugs are classified into therapeutic classes and a price is set based on a reference drug in each class. The reference price is often the lowest price drug in the class. If the physician and consumer select the reference drug, no payment is required over the standard copayment. If a drug is selected above the reference price, the consumer pays the difference in price. The objective is to have manufacturers compete to be the reference price drug and drive prices down. The manufacturer's incentive is to win market share and not to be locked out from large markets. Since the marginal cost of drug production (the cost of producing more pills) is low, it is theoretically better for manufacturers to sell at reduced prices than not to sell at all. The most expensive costs, research and development, have already been spent (and thus are sunk costs), so in theory the manufacturer will try to get as much revenue as possible as long as price exceeds marginal cost. Such price reductions could have a negative effect on the research and development of new drugs.

The key to reference pricing is what is included in each category. If categories are narrow, including only generics or exact replicas, there will be lots of categories including multiple options for treating similar conditions. Consumers and physicians will have a wide choice of drugs, but cost savings will be limited. If drug classes are broad, including all medicines that treat a particular illness, there will be fewer categories. Here,

choices are limited, but greater savings can be achieved. However, consumers with lower incomes will be more apt to forego newer, more expensive drugs. The solution might be to use sound evidence-based research to determine comparability of drugs within a class, but this research is often not available and is costly to obtain. There must also be provisions for exceptions for people who, for some reason, cannot take the reference drug.

1. Reference pricing in Germany

Germany was one of the first countries to implement reference pricing. In 1989 they introduced category one reference pricing for 10 drugs that have identical active substances — generics. The reference price was set at that of the least expensive drug, and consumers of brand name or more expensive generics would pay the difference (copayments were eliminated for this category). In 1990 and 1991, 62 more drugs were added to this system. In 1991 category two drugs (those having similar therapeutic substances) were categorized and the lowest cost drug was set as the reference price. In 1992 a reference price was set for category three drugs (those with similar therapeutic effect). In 1993 and 1994, pharmaceutical producers and physician groups were held liable for expenditures in excess of set annual budget (Zwiefel, Crivelli 1996).

Category one groupings showed an immediate shift in the price of alternative generics to the reference price. Sixty percent of brand name drugs were reduced to the reference price, and the remaining 40 percent reduced prices somewhat. Zwiefel and

Crivellie report that results of the 1993 and 1994 law changes showed industry moved more brand names to the reference price.

2. Reference Pricing in British Columbia, Canada

In 1995, British Columbia, Canada started a drug reference pricing system similar to Germany's. It began by phasing in three categories or therapeutic classes. The first category was for histamine-2 receptor antagonists (H2RA), which ranged in price from Cdn\$4.20 per month for cimetidine to Cdn\$28.20 per month for nizatidine. The reference price was set for cimetidine and the costs were covered in full without copayment. Physicians prescribing alternatives were asked for justification and exemptions were given for legitimate reasons for using other products. Consumers also had the option of paying the difference between the cost of alternatives and cimetidine (Maclure, Nakagawa et. al. 2001).

The program faced strong opposition from drug manufacturers, and physicians were concerned about losing autonomy. Maclure et. al. (2001) credited successful implementation to: an incremental approach, education of physicians and the public, quality and research based standards, an open and fair exemption process, and ongoing input from researchers in the field. Initial detailed controlled studies, conducted by the University of Washington and McMaster University along with Dr. Stephen Soumerai from Harvard, are expected in the next year. Preliminary government projections

estimate an annual cost savings of Cdn\$44 million from the program (Maclure, Nakagawa et. al. 2001).

E. Generics

Since Hatch-Waxman in 1984, there has been a proliferation in the availability and use of generics. The percent of prescribed generic drugs increased from 13 percent of the market in 1984, to 33 percent in 1993, to 45 percent of all drugs in 1998 (Kaiser 2000). Before Hatch-Waxman, there was only a 35 percent chance that a generic would be available for a top-selling drug. Today nearly every top selling off-patent drug has a generic equivalent (CBO 1998). The Congressional Budget Office reports that in 1994, generics purchased at retail pharmacies saved consumers between \$8 and \$10 million (CBO 1998).

Frank and Salkever (1997) examined the effect of generics on brand name drugs and concluded that generics do not reduce the price of brand name drugs. In fact, they lead to a slight increase in the original product. Since generics are offered at a significantly reduced price and capture a considerable share of the brand-name products market share, the net effect is a reduction in price for off-patent prescription drugs. In other words, the introduction of a generic in a particular class of drugs reduces the total amount of spending on prescriptions in that class.

Generics can play a greater role in cost reduction when combined with incentives, formularies, and reference pricing as previously described. The number of PBMs that always require generics increased from seven percent in 1995 to 29 percent in 1998 (Wyeth 1999, reported by Kreling 2000). Kreling reports that the long-term cost saving effects of generics are positive but must be balanced against a potential reduction in the rate at which new (more expensive and potentially better) drugs enter the market.

F. Disease Management

The goal of disease management is to closely monitor patient's treatment to insure that the total mix of treatment is effective and efficient. These efforts can lead to better quality at lower costs. For example, closely monitoring the drug use of asthma and diabetes patients has been shown to keep people healthier and prevent more costly emergency room visits or hospitalizations in the short and long term. Under this model, drug costs are not examined in a vacuum, and an increase in the cost of prescription drugs could lead to a decrease in costs for total health services. Seventy-six percent of HMOs and 75 percent of PBMs have disease management programs (Kreling 2000). Very little data exist evaluating the effects of disease management programs, but HMO medical directors are in agreement that these programs both improve care and reduce costs (Kreling 2000).

VII. INTERNATIONAL COMPARISONS

Other nations that provide prescription drug coverage tend to regulate price, while the United States has a mix of government regulation (patent laws, safety and efficacy standards, Medicaid law) and market forces (manufacturers, wholesalers, and retailers set price, and organized purchasers extract discounts and rebates). Price comparisons between nations are complicated by differences in dosages, strength, consumption patterns, regulations, and currencies (Danzon 1996, 1999). For example, Danzon found that drug prices in Japan were eight percent less expensive per dose than in the U.S., but 28 percent more expensive per gram of active ingredient. Caution must also be taken not to compare prices at different stages of distribution (production, wholesale, and retail) and to neglect the impact of discounts and rebates.

The GAO published studies showing drug prices in the United States were generally 32 percent higher than in Canada and 60 percent higher than in the United Kingdom. The study on Canada looked at wholesale prices of 121 drugs in both countries and found that 81 percent were more expensive in the United States. Twenty-three percent of these drugs were at least 100 percent more expensive in the United States (GAO 1992). Since the Canadian study does not take into consideration rebates and discounts and the fact that different people pay different prices, the 32 percent difference has to be viewed with caution.

OECD data showed that the United States spends less as a percentage of total health care dollars on prescription drugs than 12 other countries. In 1997 the US spent 7.8 percent compared to 20 percent for Japan, 17.3 percent for the United Kingdom, and 12.6 percent for Canada. These numbers reflect the much higher base health care spending in the U.S. compared to other industrialized nations. When examining per capita spending for pharmaceuticals, the U.S. ranks fourth (\$319 American dollars) behind France (\$351), Japan (\$348), and Belgium (\$321) (Berndt 2000).

Clearly more study needs to be done to obtain true international comparisons including the economic value of drugs purchased and the role of price controls on research and development. The GAO and other studies demonstrate, with their noted difficulties, that individual Americans, particularly those without insurance, pay higher prices for particular prescriptions. News media report on busloads of seniors in Northern states purchasing their prescriptions in Canada, and people in southern states stepping over the boarder to Mexico for discount drug prices. Congress introduced and almost passed legislation relaxing restrictions on re-importing prescription drugs from other countries in an effort to obtain short-term consumer discounts and long-term price concessions.

In 1997 South Africa passed legislation enabling it to import or manufacture generic versions of AIDS drugs currently on patent. The response of brand name pharmaceutical companies was to sue South Africa. Recently, Cipla, an Indian manufacturer applied for permission to sell cheap version of patented AIDS medication

(New York Times March 9, 2001). Merck and other manufacturers responded to the negative publicity of the lawsuit and challenges from generics by offering some of its AIDs drugs at greatly reduced prices. The New York Times reported the price of Crixivan was reduced from \$6,016 per patient per year (the U.S. price) to \$600 per patient per year, and Stocrin from \$4,730 to \$500. \$600 per patient per year just happens to coincide with the price the Cipla offered for its generics. The Sudan has already reached agreement with manufacturers for deep discounts.

These cases demonstrate the complexity of international trade in lifesaving pharmaceuticals. It is difficult for countries to adhere to patent law when the result is the death of their citizens . But what is the long-term effect of countries bypassing patent law? Is it equitable for drugs to be priced the same for all countries? Do first world countries have responsibility to subsidize drug purchases in the third world? Do drug companies have an obligation to sell their products at reduced prices to people and nations that cannot afford lifesaving medicine? These are difficult tradeoffs currently being worked out by nations and global pharmaceutical manufacturers and distributors.

An examination of international comparisons raises many questions and challenges. First, it is difficult methodologically to make international comparisons. Second, cost controls in smaller market countries may not have as much impact on research and development as price controls in larger markets. These nations benefit from research and development without paying the full costs, but it is still profitable for manufacturers to sell in these markets (marginal cost of production is low). Third, it may

not be a bad thing to sell drugs at a cheaper cost to nations with fewer resources.

Alternatively, first world nations could contribute to help purchase lifesaving medicine.

VIII. CONCLUSION

The economics of drug pricing in the United States is characterized by a complex mix of regulation and market competition. Health expenditures for prescriptions have been rising more rapidly than for any other type of medical care. The net effect of this, however, remains unclear. The development of new products, increased use and demand, and the growing number of people with prescription drug insurance are pushing up costs. Direct-to-consumer advertising is also increasing demand. The average drug takes 12 years and cost \$270 million dollars to bring to market. Hatch-Waxman and GATT together increased the real patent protection period, but because of the wide variation in profitability for particular drugs, determining the appropriate level of patent protection is difficult.

Some complain that pharmaceuticals are making excessive profits, while others claim that profits are average when taking into consideration high research and development costs. Pharmaceuticals companies in the United States have a greater ability to set price than in other industrialized nations. New innovative drugs come into the market with high demand and high costs. New drugs with close substitutes come into the market with low prices and try in order to gain market share. Organized purchasers are able to extract price discounts, but the uninsured or underinsured (particularly senior

citizens) do not benefit from these discounts and some have problems obtaining needed prescriptions.

Caution must be taken when seeking to restructure part or all of the market. Pharmacy benefit managers (PBMs), Medicaid, and the VA have deployed successful strategies to contain costs for their members, but the effect on the overall market is uncertain. Cost sharing strategies make consumers more price sensitive and limit moral hazard, but even small cost sharing leads some to go without necessary medication. Rebates and discounts are given for steering market share to particular products or distribution networks, but are generally not available for generics or innovative new products. Reference pricing shows signs of success in Germany and British Columbia, Canada. The key question is how narrow or wide drug categories are constructed – too narrow and price savings are modest, too wide and access to drugs for people with limited income is reduced. A greater use of generics will save money, but allowing generics in the market too early may reduce incentives to develop new, innovative drugs. Disease management holds real possibilities for long term efficiencies, but cost savings are still uncertain. International comparisons are difficult to make, but provide clear examples of how differences in purchasing power can influence drug pricing and distribution. All of these issues and trade-offs must be considered by legislators in formulating future policy.

References

- Angus, D.E., and H.M. Karpetz (1998). "Pharmaceutical Policies in Canada: Issues and Challenges," *PharmacoEconomics*, 14, Supplement 1, 81-96.
- Barens Group LLC (1999). Factors affecting the growth of prescription drug expenditures. Washington: NIHCM Foundation.
- Berndt, E.R., Cockburn, I.M., and Z. Griliches (1996). "Pharmaceutical Innovations and Market Dynamics: Tracking Effects on Price Indexes for Antidepressant Drugs," in *Brookings Papers on Economic Activity*, Special Issue, 133-199.
- Berndt ER, Cockburn IM, Cocks DL et al (1997). Is price inflation different for the elderly? National Bureau of Economic Research working paper 6182. Forthcoming in Garber A, *Frontiers of Health Policy*.
- Berndt, Ernst, R. (2000) "The U.S. Pharmaceutical Industry: Why Significant Growth in Times of Cost Containment?" MIT Sloan School of Management, National Bureau of Economic Research, January.
- Bloom, BS and Jacobs, J. "Cost effects of restricting cost-effective therapy." *Medical Care* 1985;23(7): 872-80.
- Brealey and Myers, (2000) *Principles of Corporate Finance*, Part Three "Practical Problems in Capital Budgeting.
- Cook, A. Kornfield, T. and Gold, M. "Role of PBMs in Managing Drug Costs: Implications for a Medicare Drug Benefit," *Mathematica Policy Research*, January 2000.
- Cook, Anna (2000). "Why Different Purchasers Pay Different Prices for Prescription Drugs." A Background Report Prepared for the Department of Health and Human Resources Conference on Pharmaceutical Pricing Practice, Utilization and Cost. Washington DC. August 8-9.
- Copeland, C. (1999). "Prescription Drugs: Issues of Cost, Coverage, and Quality." **Employee Benefit Research Institute April (208): 1-21.**
- Committee on Government Reform, (1999) "Prescription Drug Pricing in the United States: Drug Company Profit at the Expense of Older Americans." Prepared for Rep. Henry Waxman, Minority Staff Special Investigations Division, Committee on Governmental Reform, U.S. House of Representatives. November 9.
- Congressional Budget Office (CBO) (1998) "How Increased Competition From Generic Drugs has Affected Prices and Returns in the pharmaceutical Industry" <http://www.cbo.gov/execsum.cfm?index=1&from=1&file=exsum.htm> July.
- Danzon, P.M. (1996). "The Uses and Abuses of International Price Comparisons," in R.B. Helms (ed.), *Competitive Strategies in the Pharmaceutical Industry*, Washington DC: AEI Press, 85-106.
- Danzon, P.M., and J.D. Kim (1998). "International Price Comparisons for Pharmaceuticals," *PharmacoEconomics*, 14, Supplement 1, 115-128.
- Danzon, P.M. (1999). *Price Comparisons for Pharmaceuticals: A Review of U.S. and Cross-National Studies*, Washington, DC: AEI Press.
- Davis, M., J. Poisal, et al. (1999). "Prescription Drug Coverage, Utilization, and Spending Among Medicare Beneficiaries." *Health Affairs* 18(1): 231-243.

- DiMasi, Joseph, A. (2000) "Price Trends for Prescription Drugs: 1995-1999" A Background Report Prepared for the Department of Health and Human Resources Conference on Pharmaceutical Pricing Practice, Utilization and Cost. Washington DC. August 8-9.
- Drummond MF et al. *Methods for the Economic Evaluation of Health Care Programmes*. Oxford: Oxford University Press, 1997.
- Dubois RW, Chawla AJ, Neslusan CA et al. (2000). Explaining drug spending trends: Does perception match reality? *Health Affairs* 19(2): 231-239.
- Dubois, R.W., Chawla, A.J., Neslusen, C.A., Smith, M.W., and S. Wade (2000). "Explaining Drug Spending Trends: Does Perception Match Reality?," *Health Affairs*, 19(2), 231-239.
- ExpressScripts (1999). Drug Trend Report, 1998. Express Scripts: Maryland Heights, Missouri.
- Families U.S.A., (2000) Pollack, Ron, "The Affordability of Pharmaceuticals" Presented at the Seventh Princeton Conference, Council on the Economic Impact of Health System Change. May 11- 13, 2000.
- Frank, Richard, G. and Salkever, David, S. (1997) "Generic Entry and the Pricing of Pharmaceuticals" *Journal of Economics and Management Strategy*, (Vol. 6 Nos. 1, Spring 1997) 75 – 90.
- General Accounting Office. Prescription Drug Benefits: Implications for Beneficiaries of Medicare HMO Use of Formularies. Washington, D.C., General Accounting Office. 1999a.
- General Accounting Office. VA's Management of Drugs on its National Formulary. Washington, D.C., General Accounting Office. 1999b.
- Gluck, M. (2000). "A Medicare Prescription Drug Benefit" National Academy of Social Insurance, Medicare Brief, April, 1999: 1-14
- Goldberg, Robert (1999). Ten myths about the market for prescription drugs. National Center for Policy Analysis: Washington DC. Policy Report No. 230.
- Grabowski, H. and Mullins, C. (1997) "Pharmacy Benefit Management, Cost Effectiveness Analysis, and Drug Formulary Decisions," *Social Science and Medicine* 45, no. 4 (197)L 535-544.
- Grabowski, Henry, G. and Vernon, John, M. (2000) "Effective Patent Life in Pharmaceuticals" *International Journal of Technology Management* (Vol. 19 Nos. 1/2),. 98 - 120.
- Griliches, Z., and Cockburn I.M. (1996). "Generics and the Producer Price Index for Pharmaceuticals," in *Competitive Strategies in the Pharmaceutical Industry*, Washington DC: AEI Press, 19-34.
- HCFA (2000). National health expenditures tables. Health Care Financing Agency: Washington DC. Accessed 3/20/00 from <http://www.hcfa.gov/stats/nhe-oact/tables/Tables.pdf>
- Huskamp, Haiden, A. et. al. (2000) "How Will Medicare Play the Game" *Health Affairs* 2000;19(2): p 8-23.
- Kalorama (2000). Psychotherapeutic drugs. Kalorama Information LLC: Bethesda, MD.
- Kaiser Family Foundation, (2000) "Prescription Drug Trends: A Chartbook" Menlo Park, California, July.
- Kleinke, J.D. (2000), "The Paradox of Rising Drug Costs" *Health Affairs* 2000;19(2): 78-91

Kreling, David, H. (2000) "Cost Control for Prescription Drug Programs: Pharmacy Benefit Manager (PBM) A Background Report Prepared for the Department of Health and Human Resources Conference on Pharmaceutical Pricing Practice, Utilization and Cost. Washington DC. August 8-9.

Kordella, R. (1999). What's Driving Rx Cost Increases (And What Can Your PBM Do About It?). 1999.

Kozma, CM, Reeder, CE and Lingle, EW. "Expanding Medicaid drug formulary coverage. Effects on utilization of related services." *Med Care* 1990;28(10): 963-77.

Johnson, R. E., M. J. Goodman, et al. (1997). "The Effect of Increased Prescription Drug Cost-sharing on Medical Utilization and Expenses of Elderly Health Maintenance Organization Members." *Medical Care* 35(11): 1119-1131.

Johnson, R. E., M. J. Goodman, et al. (1997). "The Impact of Increasing Patient Prescription Drug Cost Sharing on Therapeutic Classes of Drugs Received and on Health Status of Elderly." *Health Services Research* 32(1): 103-122.

Lehmann, DF. "Effect of a prior-authorization requirement on the use on nonsteroidal antiinflammatory drugs by Medicaid patients [letter]." *N Engl J Med* 1995;333(19): 1289.

Leibowitz, A., W. G. Manning, et al. (1985). "The Demand for Prescription Drugs as a Function of Cost-Sharing." *Social Science and Medicine* 21(10): 1063-1069.

Lu, John, Z., Comanor, William, S., (1998) "Strategic Pricing of New Pharmaceuticals" The Review of Economics and Statistics, (Harvard College and Massachusetts Institute of Technology) 108 – 118.

Mathematica Policy Research, Inc. (2000) "The Role of PBMs in Managing Drug Costs: Implications for a Medicare Drug Benefit." Paper presented at the Seventh Princeton Conference, Council on the Economic Impact of Health System Change, Access to Pharmaceuticals, May 11-13.

Manning R.L. (1997). "Products Liability and Prescription Drug Prices in Canada and the United States," *Journal of Law and Economics*, 40, 203-243.

McClure, Malcolm, et. al. (2001) "Applying Research to the Policy Cycle: Implementing and Evaluating Evidence-Based Drug Policy in British Columbia (Advanced copy obtained by the Council, March)

Merlis, Mark. (2000). "Explaining the Growth in Prescription Drug Spending: A Review of Recent Studies" A Background Report Prepared for the Department of Health and Human Resources Conference on Pharmaceutical Pricing Practice, Utilization and Cost. Washington DC. August 8-9.

Mott, D. A. and D. H. Kreling (1998). "The Association of Insurance Type with Cost of Drug Dispensed." *Inquiry* 35(Spring): 23-35.

Mueller, C., Schur, C., and O'Connell, J. (1997). "Prescription Drug Spending: The Impact of Age and Chronic Disease Status." *American Journal of Public Health* Oct; 87 (10): 1626-1629.

Neumann PJ, Sandberg EA, Bell CM, Stone PW, Chapman RH. Are pharmaceuticals cost-effective? A review of the evidence. *Health Affairs* 2000;19(2): 92-109.

Newcomber, Lee N. Medicare Pharmacy Coverage: Enjoying Safety Before Funding," *Health Affairs*, 19(2):49-62, March/April 2000.

Palumbo, Francis and Mullins, Daniel, C. (2000) "Projections of Drug Approvals, Patent Expirations, and Generic Entry from 2000 to 2004" A Background Report Prepared for the Department of Health and Human Resources Conference on Pharmaceutical Pricing Practice, Utilization and Cost. Washington DC. August 8-9.

Reinhardt, Uwe E. "Prescription Drugs: Addressing Cost, Coverage and Quality" Presented at the Fourth Annual NCSL Health Conference, Charlotte, North Carolina, December 1-3, 2000.

Reekie, W.D. (1978). "Price and Quality Competition in the United States Drug Industry," *Journal of Industrial Economics*, 26, 223-237.

Reekie, W.D. (1998). "How Competition Lowers the Cost of Medicines," *PharmacoEconomics*, 14, Supplement 1, 107-113.

Segedin B et. al (1999). "Three-tier Co-payment plans: Design Considerations and Effectiveness *Drug Benefit Trends* 11 September, p. 43-52.

Shulman, S.R., DiMasi, J.A., and K.I. Kaitin (1999). "The Impact of the Waxman-Hatch Act on New Drugs and Biologics Approved 1984-1995," *Journal of Biomedicine and Business*, 2(4), 63-68.

Smalley, WE, Griffin, MR, Fought, RL, Sullivan, L and Ray, WA. "Effect of a prior-authorization requirement on the use of nonsteroidal antiinflammatory drugs by Medicaid patients." *N Engl J Med* 1995;332(24): 1612-7.

Smith, D. G. (1993). "The Effects of Copayments and Generic Substitution on the Use and Costs of Prescription Drugs." *Inquiry* 30(2): 189-198.

Soumerai, S. B., J. Avorn, et al. (1987). "Payment Restrictions for Prescription Drugs Under Medicaid." *The New England Journal of Medicine* 317(9): 550-556.

Soumerai, SB, Ross-Degnan, D, Gortmaker, S and Avorn, J. "Withdrawing payment for nonscientific drug therapy. Intended and unexpected effects of a large-scale natural experiment." *JAMA* 1990;263(6): 831-9.

Soumerai SB et al. Effects of Medicaid drug payment limits on admission to hospitals and nursing homes. *New England Journal of Medicine* 1991;325(15):1072-1077.

Soumerai SB, McLaughlin TJ, Ross-Degnan D, Casteris CS, Bollini P. Effects of limiting medicaid drug-reimbursement benefits on the use of psychotropic agents and acute mental health services by patients with schizophrenia. *New England Journal of Medicine* 1994;331:650-655.

Soumerai, S. B., D. Ross-Degnan, et al. (1997). "Determinants of Change in Medicaid Pharmaceutical Cost Sharing: Does Evidence Affect Policy?" *The Milbank Quarterly* 75(1): 11-34.

U.S. General Accounting Office, (1997) "Pharmacy Benefit Management: FEHBP Plans Satisfied with Savings and Service, but Retail Pharmacies Have Concerns," Pub. No. HEHS-97-47 (Washington D.C.: U.S. Government Printing Office, February 21).

U.S. General Accounting Office (1992) "Prescription Drugs, Companies Typically Charge More in the United States Than in Canada" Pub. No. HRD-92-110 (Washington D.C. U.S. Printing Office, September).

U.S. General Accounting Office (2000) "Expanding Access to Federal Prices Could Cause Other Things to Change." Pub. No. HEHS-00-118 (Washington D.C. U.S. Printing Office, August).

Weinstein MC et al. Panel on cost-effectiveness in health and medicine. Recommendations of the Panel on Cost-Effectiveness in Health and Medicine. *Journal of the American Medical Association* 1996;276(15):1253-1258.

Wilkes Michael, S. et. al. (2000) "Direct-to-Consumer Prescription Drug Advertising: Trends, Impact, And Implications." *Health Affairs* 2000;19(2): 110-128

Wyeth-Ayerst Prescription Drug Benefit Cost and Plan Design Survey Report, 1999 Edition, Pharmacy Benefit Management Institute, Inc. (1999).

Zweifel, Peter, Crivelli, Luca, (1996), "Price Regulations of Drugs: Lessons From Germany" *Journal of Regulatory Economics*: 10: 257-273.