Pharmaceuticals

Health Economics and Policy

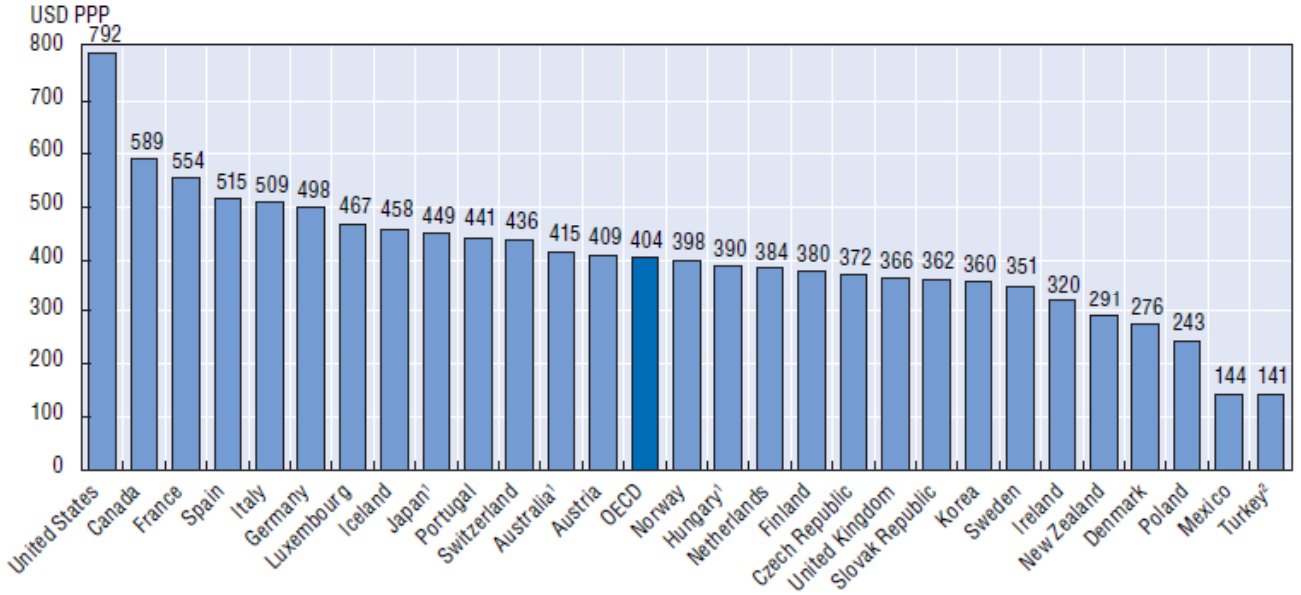
Drug Expenditures

- Per capita spending on pharmaceuticals (in USD PPP)
  - In 2005: US 792; Canada 589; France 554; Germany 498; UK 366; OECD 404
- Pharmaceutical expenditures as percentage of national health expenditures
  - In 2003: US 12.9; Canada 16.9; France 20.9; Germany 14.6; OECD 17.8

Drug Expenditures

Figure 1.2. **Per capita spending on pharmaceuticals, 2005**

In USD PPP



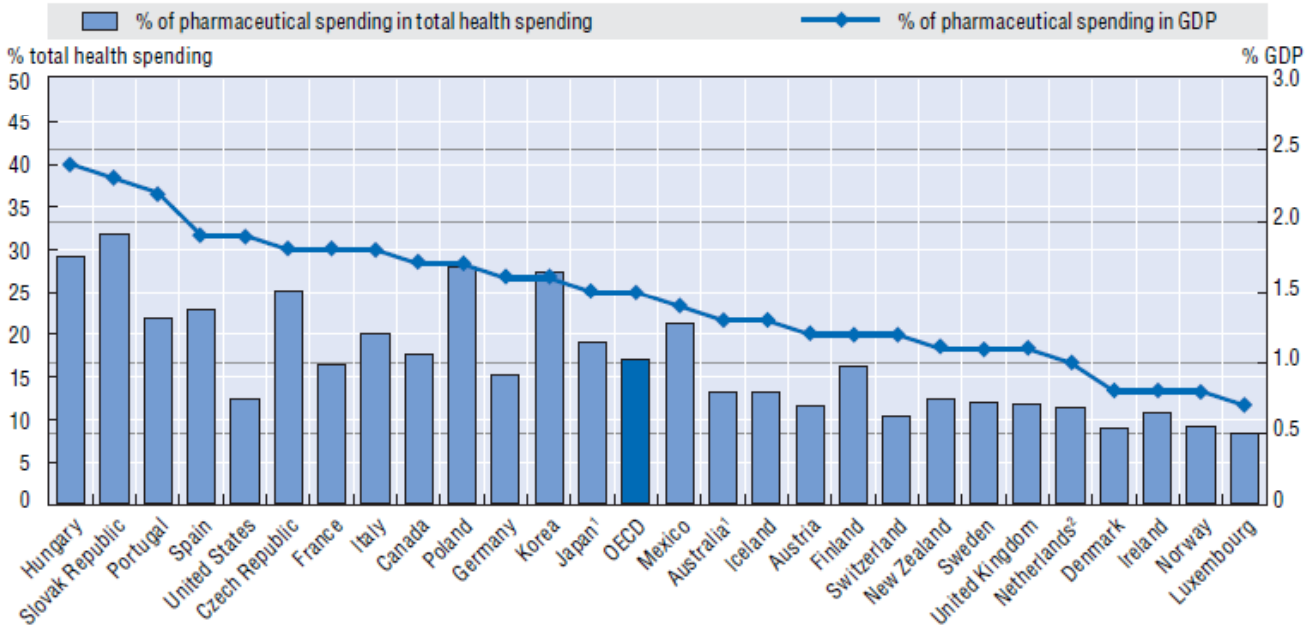
Note: Expenditures were converted from national currency units to US dollars using GDP purchasing power parities. See Box 1.1 for more notes.

1. 2004 (Japan and Hungary) and 2004/05 fiscal year (Australia).
2. Data reported are 2005 pharmaceutical sales at ex-manufacturer prices, which underestimate total pharmaceutical expenditure.

Source: *OECD Health Data 2007* and authors' estimates. See Box 1.1 for more sources.

Drug Expenditures

Figure 1.5. **Share of pharmaceutical expenditure in total health spending and in GDP, 2005**



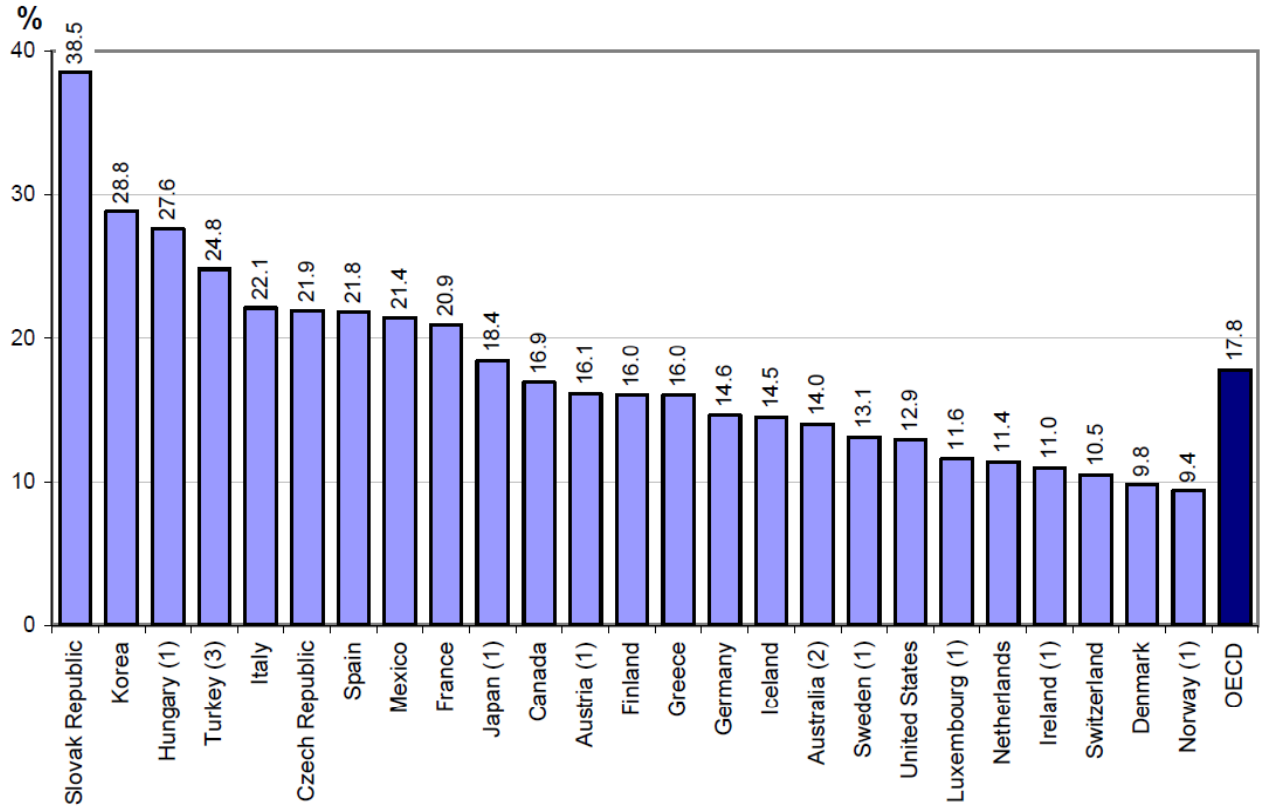
Note: See Box 1.1 for more notes.

1. 2004 (Japan) and 2004/05 fiscal year (Australia).
2. 2002.

Source: OECD Health Data 2007, except total health expenditure for the United Kingdom (Office for Health Economics Compendium of Health Statistics 2007, estimate for total health expenditure from Table 2.1). See Box 1.1 for more sources.

Drug Expenditures

Chart 2. Drug expenditure as percentage of total health spending, 2003

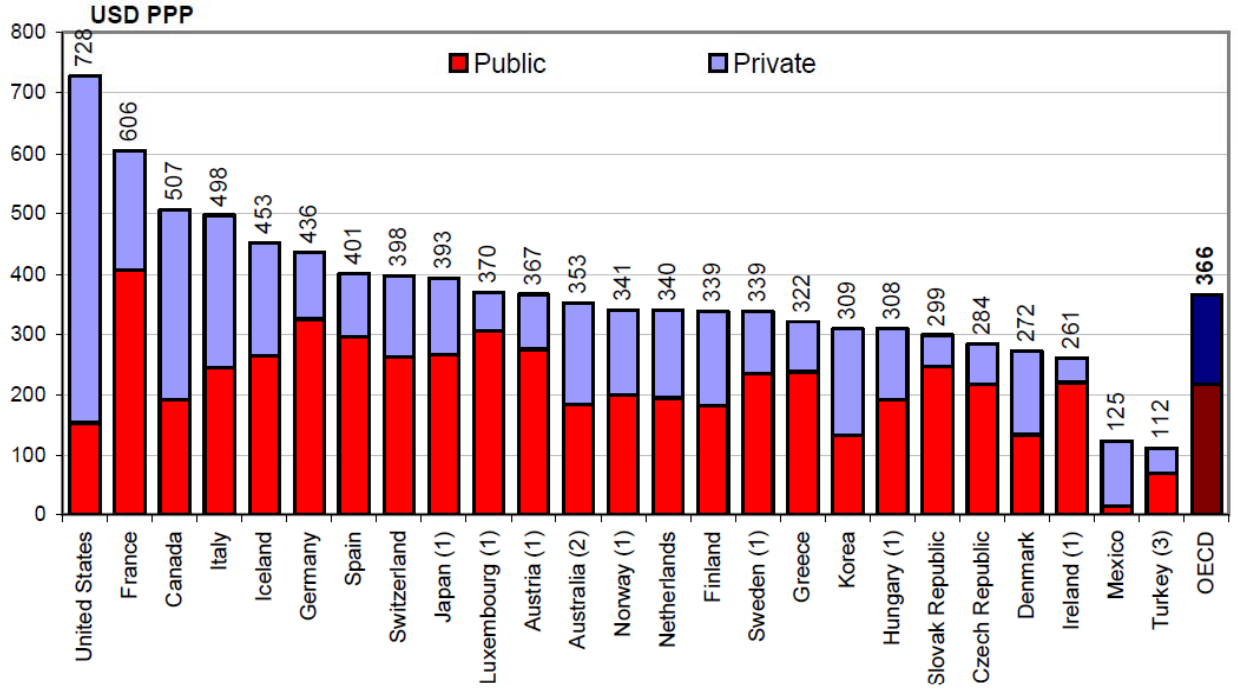


(1) 2002. (2) 2001. (3) 2000.

Source OECD HEALTH DATA 2005. June 05

Drug Expenditures

Chart 3. Drug expenditure per capita, public and private spending, 2003



Data are expressed in purchasing power parities (PPPs), which provide a means of comparing spending between countries on a common base. PPPs are the rates of currency conversion that equalise the cost of a given 'basket' of goods and services in different countries.

(1) 2002. (2) 2001. (3) 2000.

Source OECD HEALTH DATA 2005, June 05

Drug Expenditures

- Expenditures – rising rapidly in recent years
  - Significant growth in pharmaceutical expenditures in many countries
  - Fastest growing component of overall health care spending
  - Increase in prescription drug expenditures due to …
    - Price?
    - Utilization?
    - Quality?

Drug Expenditures

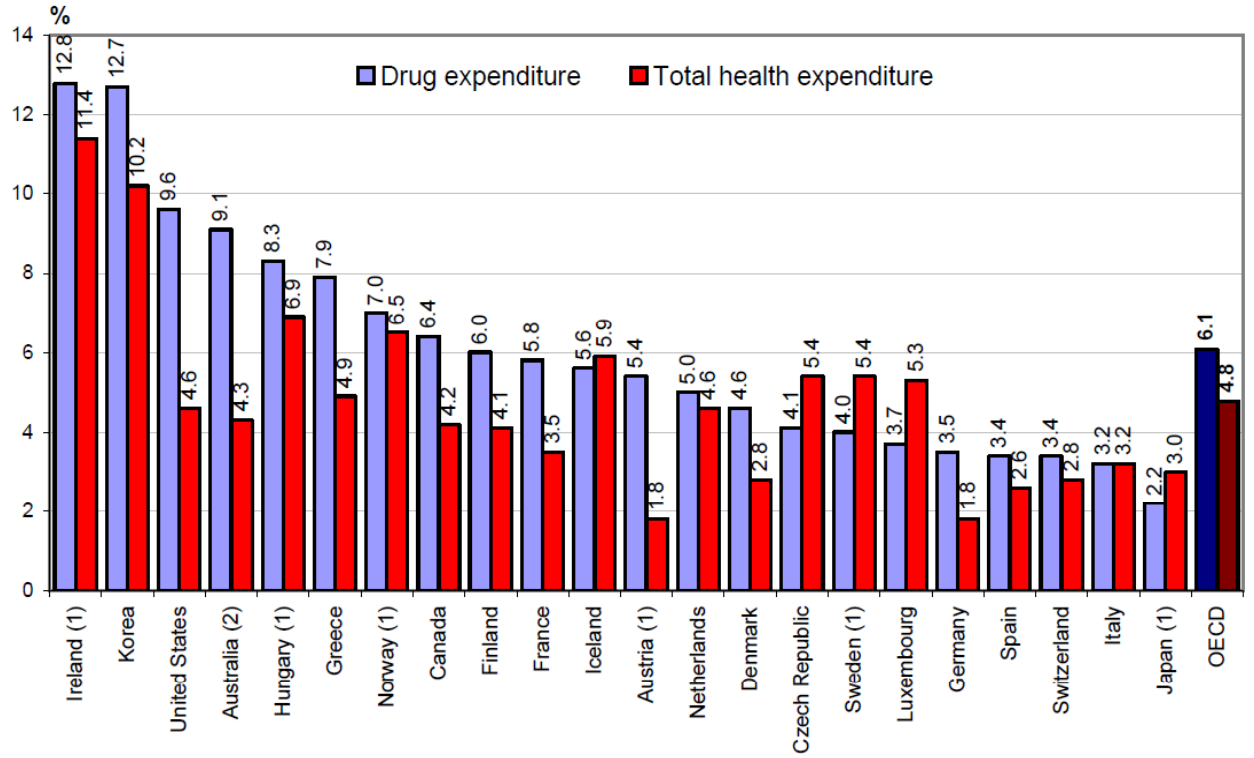
Global Pharmaceutical Sales 2000 – 2007

	2000	2001	2002	2003	2004	2005	2006	2007
Total World market (current US$)	365	392	428	499	560	605	649	**712**
Growth Over Previous year ($Constant US$ Growth)	11.5%	11.8%	9.5%	10.3%	8.0%	7.3%	7.1%	**6.4%**

Source: IMS Health Market Prognosis (includes IMS Audited and Unaudited markets)
All information current as of March 28, 2008

Drug Expenditures

Chart 1. Annual growth in drug expenditure and in total health expenditure, 1998 to 2003



Note: Countries are ranked from left to right by annual growth of per capita pharmaceutical expenditure.

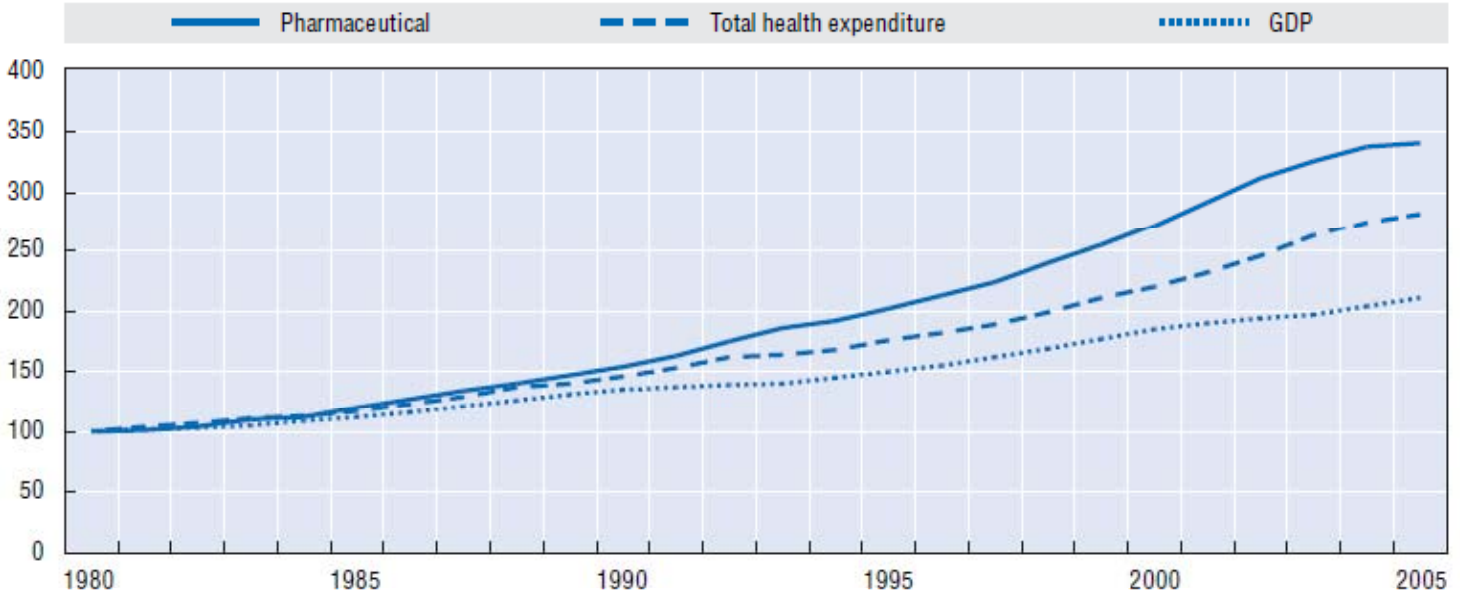
(1) 1998-2002. (2) 1997-2001.

Source OECD HEALTH DATA 2005, June 05

Drug Expenditures

Figure 1.7. **Trend growth in pharmaceutical and total health expenditure for 15 OECD countries, and GDP, 1980-2005**

1980 = 100



Note: Indexes were calculated using national currency units at 2000 GDP prices. Pharmaceutical expenditure is excluded from total health expenditure.

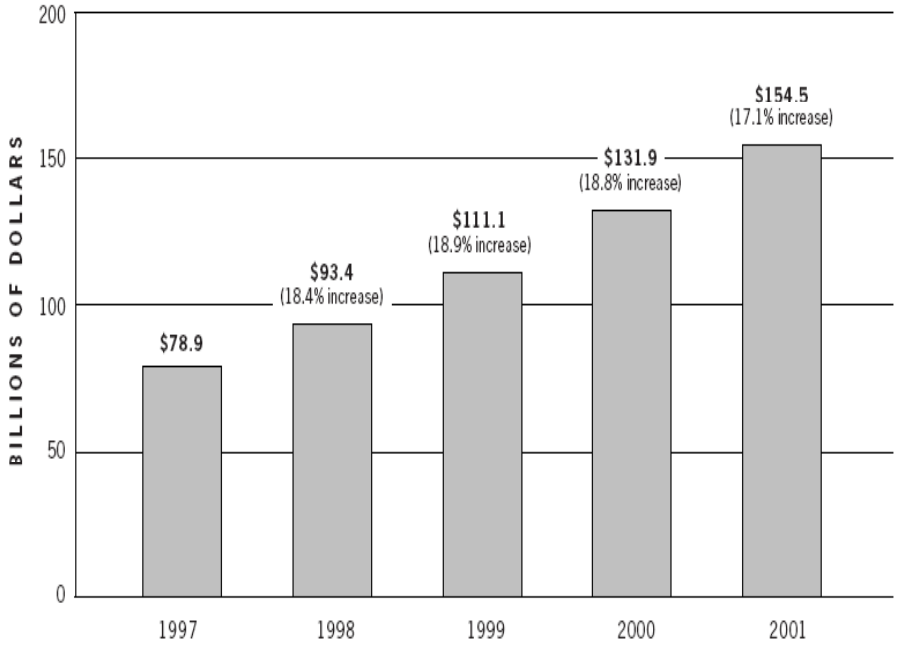
Source: OECD Health Data 2007.

Rising Prescription Drug Expenditures (Example from US)

- Prescription drug expenditures rising over the years (between 1999 and 2000 increased by 17.3%, reaching $122 billion – source CMS). Fastest growing component in the health care system – twice the rate of all other HC services
- In 2000, prescription drug expenditures represent about 9% of total health care expenditures (hospitals 38% and physicians 23%). This is up from 5.8% in 1990 (Americans spend twice as much on computers and three times as much on cars)
- Prescription expenditures shifted from OOP to Private HI (in 1988 60% of prescription exp paid by OOP and 24% by PHI and by 2000 32% paid by OOP and 46% by PHI)
- But patients pay a higher percentage of drug expenditures out of pocket than they do for other major health expenditures (such as for hospitals etc.)
- Is rising prescription drug expenditures necessarily bad?

Prescription Drug Expenditures

FIGURE 1
Retail Spending on Prescription Drugs in the U.S.



SOURCE: American Institutes for Research (AIR) analysis of Scott-Levin data

Drug Spending as Measured by Different Groups

(BILLIONS OF DOLLARS)

	1999	2000	Percent Change
HCFA[a]	$99.6	$116.9	17.4%
NIHCM/AIR/Scott-Levin[b]	$111.1	$131.9	18.8%
IMS Health[c]	$126.3	$145.1	14.9%

SOURCES:

a. Health Care Financing Administration (*Health Affairs*, March–April 2001); 2000 projected

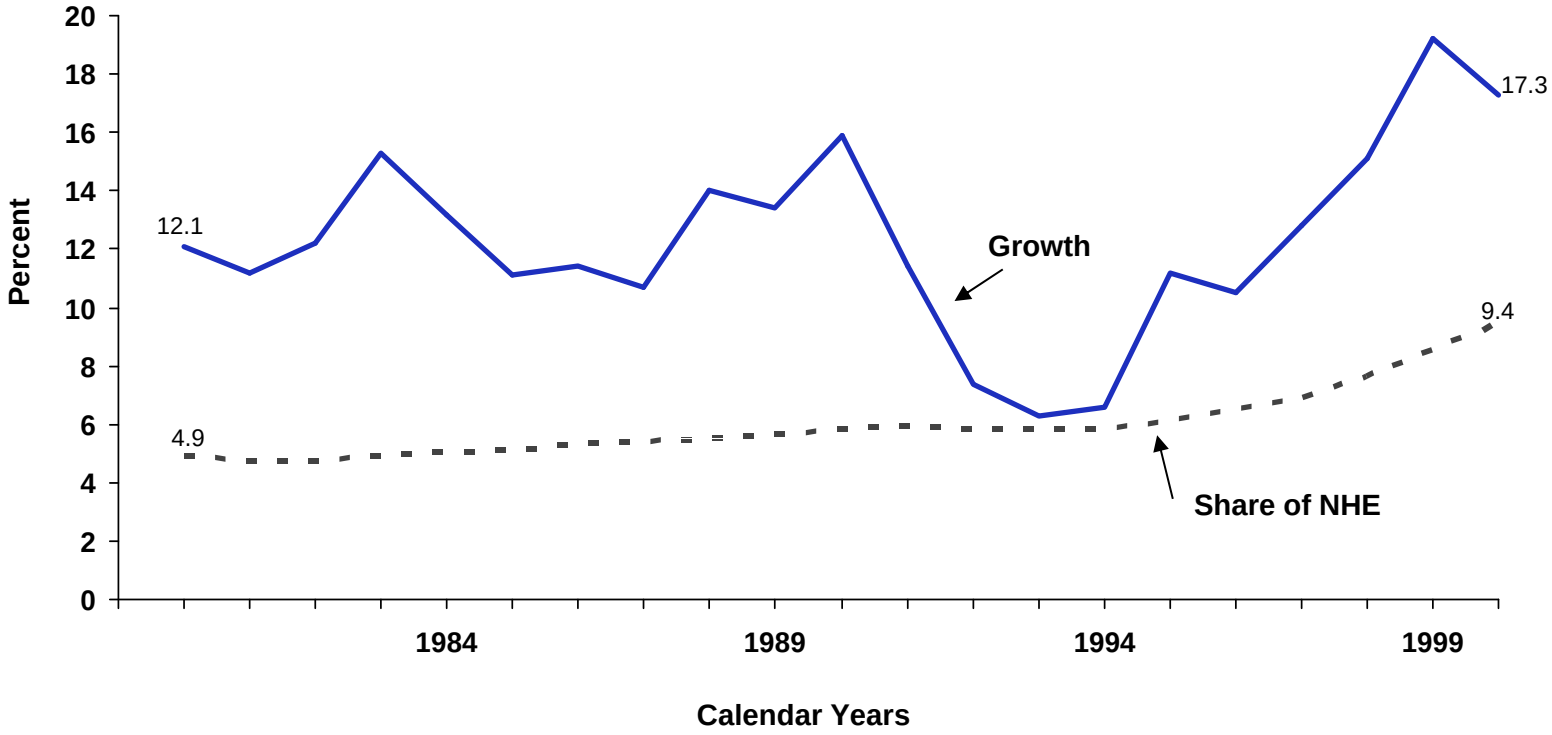
b. NIHCM/American Institutes for Research analysis of Scott-Levin Prescription Drug Audit (April 2001)

c. IMS Health, Westport, CT (February 2001)

- Between 1999 and 2000, prescription drug expenditures rose by 17.3%, reaching $122 billion (CMS figures)

Prescription Drug Expenditure Growth and Share of National Health Expenditures

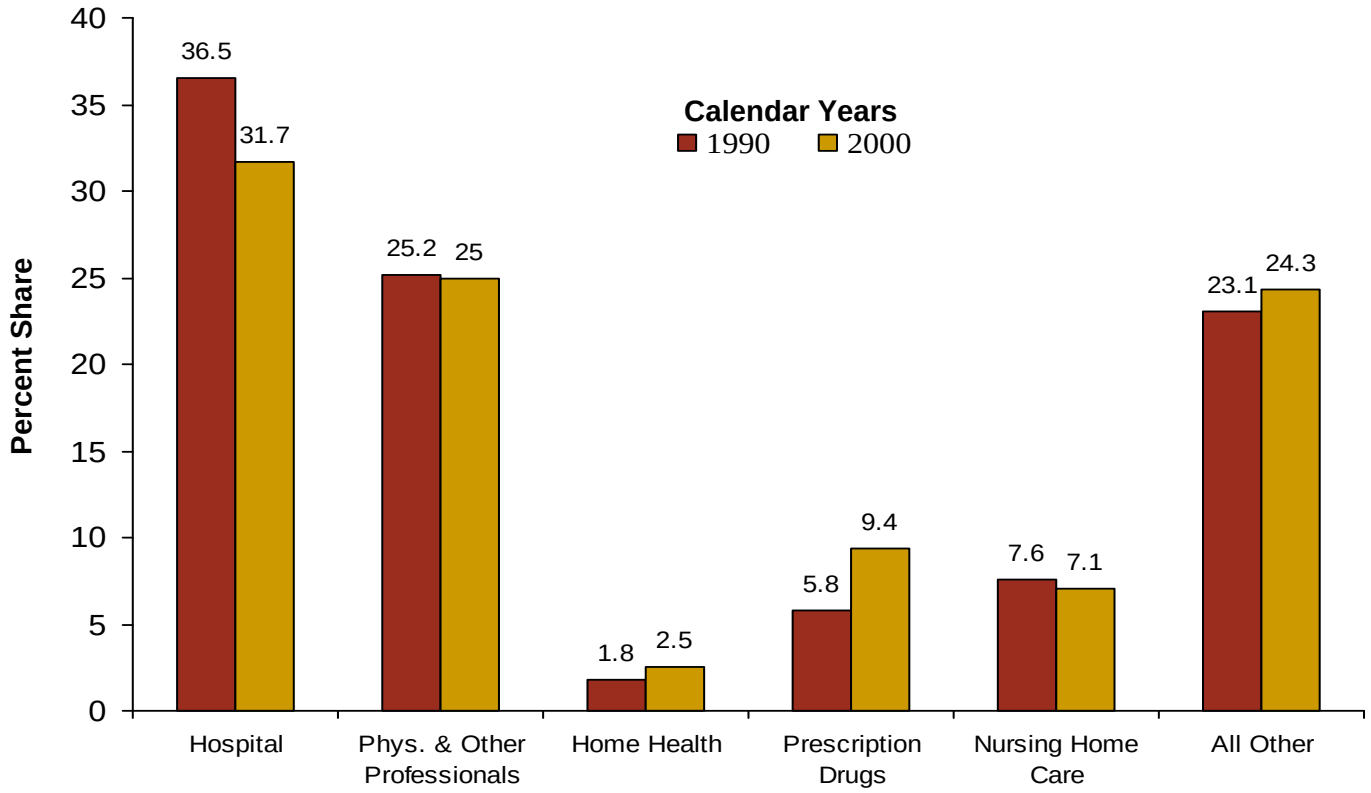
Sharply rising prescription drug expenditure growth nationwide in the mid- to late 1990s caused noticeable growth in prescription drugs as a share of total health spending.



Source: CMS, Office of the Actuary, National Health Statistics Group.

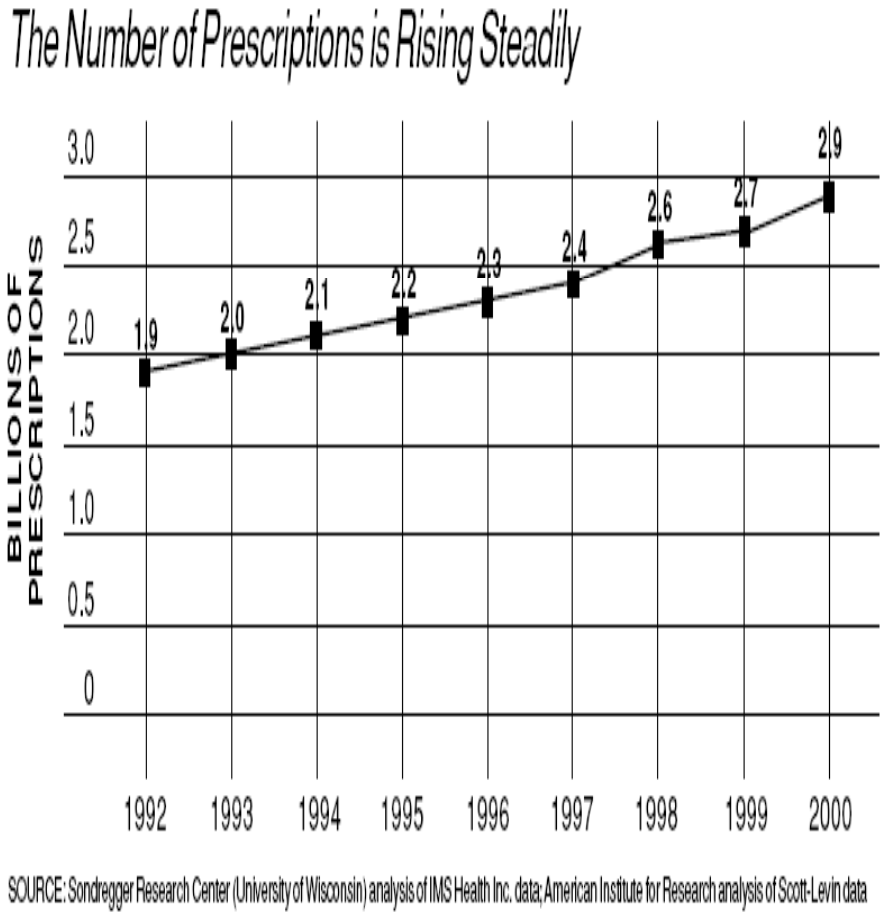
Expenditures for Health Services, by All Payers

In recent years, the hospital share of total spending has decreased while the prescription drug share has increased.



Source: Centers for Medicare & Medicaid Services, Office of the Actuary, National Health Statistics Group.

Why the rise in pharmaceutical expenditures?



- Expenditures = Price * Quantity
- Percent increase in price is relatively small
  - Annual % change in prescription drug price is between 8-10% in the 80's and between 2 and 6% (usually less than 4) in the 90's
  - BLS drug price index overstates drug price index
  - (also, price does is not quality adjusted --- which infact may show that price has not increased but may have actually decreased)
- However, prescriptions per capita as well as number of dispensed prescriptions have been rising
  - 7.3 prescriptions per capita in 1992 and 10.4 in 2000
  - 1.9 billion dispensed prescriptions in 1992 and 2.9 billion in 2000
  - For example, compared to 1999, retail pharmacies in 2000 dispensed: 42.4% more Celebrex; 73% more OxyContin; 32.3% more Lipitor 74.3% more Singular; 95% more Celexa
- Shift toward newer (and more expensive) drugs

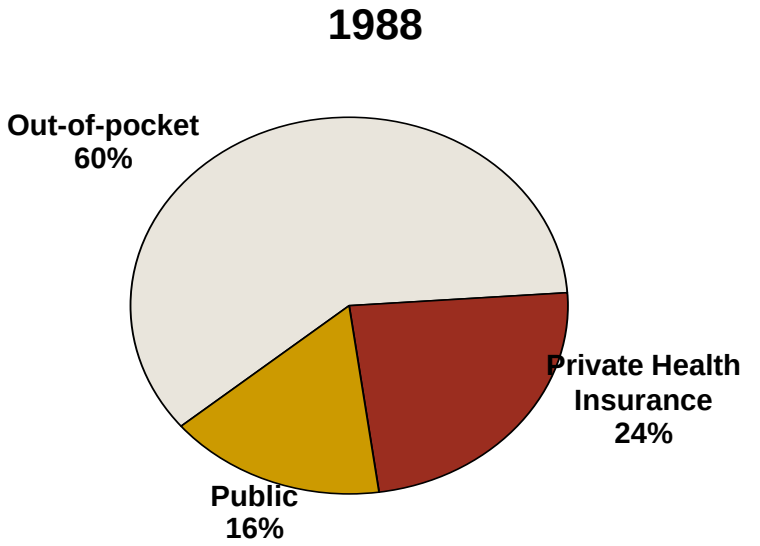
Change in Quantity due to Ageing Population

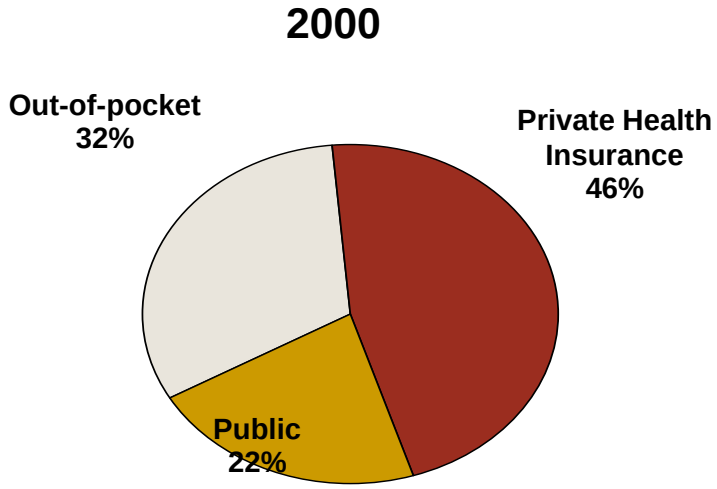
- Aging population
  - Population growth is about 1% per year but the number of aged has been increasing more rapidly
  - The aged have the highest use rate of prescription drugs

Number of prescriptions prescribed per year (1997)	1.5	2.3	6.5	9.4	11.4
Age Group	5-14	25-34	55-64	65-74	75+

Change in quantity due to increased drug coverage

- Growth in insurance coverage for prescription drugs
  - The financing of prescription drug expenditures has shifted from consumer out-of-pocket spending to private health insurance.
  - Declining drug expenditures paid by OOP:
    1970 → 82%;
    1980 → 69%;
    1990 → 59%;
    2000 → 35%;
  - Public (Medicaid and Medicare HMOs) increased from 16% to 22%
  - Private HI increased from 24% to 46%





Increase in Expenditures Due to New Drugs

- The average retail price of all prescription drugs rose 10.5% from 1999 to 2000, from $40.96 to $45.27

- Of the $4.31 increase, NIHCM attributes $1.64 to the “pure” price inflation at the manufacturer, wholesale and retail level. The remaining $2.67 is due to the “shift effect” to more expensive (and newer) drugs across the entire prescription drug marketplace (The National Institute for Health Care Management – May 2001 report)

Increase in Expenditures Due to New Drugs

Table 5. Percentage Contribution of Changes in Price and Utilization to 1993-98 Increase in Prescription Drug Spending

	Price Effect	Utilization Effect	TOTAL
New Drugs (1992 and later)	42%	23%	65%
Older Drugs	22%	13%	35%
TOTAL	64%	36%	100%

Average per year increases:

42/5 = 8.4%; 23/5 = 4.6% 65/5=13.0%;

22/5 = 4.4%; 13/5 = 2.6% 35/5=7.0%

64/5 = 12.8; 36/5 = 7.2% 100/5 = 20%

Rising Prescription Drug Expenditures

- Much of increase attributable to increases in prices
  - About 2/3 of increase attributable to price increases
  - Difficult to sort out increases in quality resulting from introductions of new, often expensive drugs
- Significant increases in prescription drug use
  - Accounts for about 1/3 of overall increase in expenditures
  - Number of prescriptions per capita up by more than 50% in 1990s
  - Introduction of variety of new "blockbuster" drugs
    - Claritin, Vioxx, Prilosec, Viagra…
    - 2/3 of increased use results from use of new drugs

Is Rising Drug Expenditures Necessarily Bad?

- New drugs can treat previously untreated conditions and many new "lifestyle" drugs (Viagra, Claritin, Prilosec and pain relievers) improve quality of life

- Replacement of older drugs by newer ones has resulted in reductions in (Lichtenberg 2002)
  - mortality,
  - morbidity (work loss days)
  - treatment costs (fewer admissions and reduced LOS)
- New drugs may reduce non-pharmaceutical expenses
  - New antidepressants reduce costly psychotherapy
  - Beta-blockers and BP drugs reduce the cost of heart related diseases requiring hospital admissions and surgeries

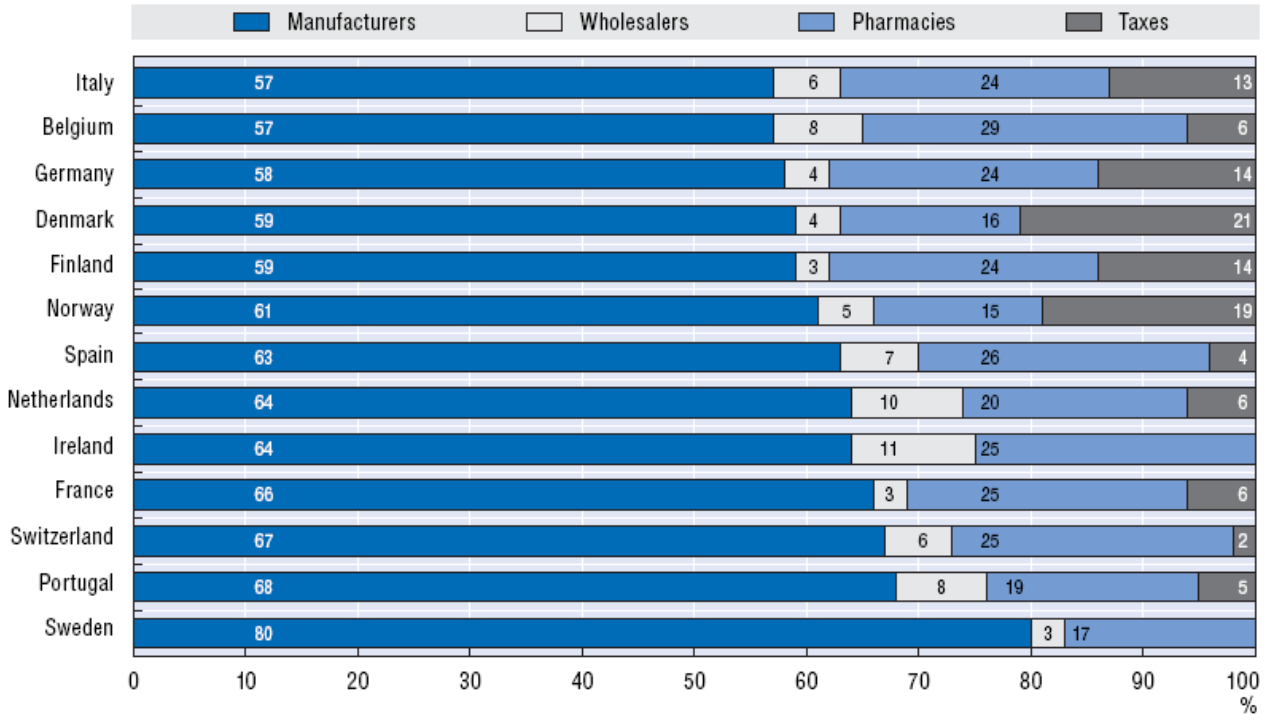
Cost of Drug Therapy Vs. Surgery

- The cost of drug treatment ranges from less than 1% to about 8% of cost of surgery for selected disease categories (Weidenbaum, 1993)
- Newly introduced drugs reduced nondrug medical spending by almost $4 for every $1 spent on drugs (89% of which is due to reduction in inpatient hospital expenses) (Lichtenberg, 2001)

Disease Category	Cost of Surgery	Cost of Drug Therapy	Drug Therapy as % of Surgery
Ulcers	$28,900	$900	3.1
Heart Disease	43,370	300	.7
Gallstones	12,000	1,000	8.3
Source: Weidenbaum (1993)			

Components of Retail Pharmaceutical Prices

Figure 1.9. **Components of retail pharmaceutical prices, selected OECD countries, 2004**



Source: VFA (2006), The *Pharmaceutical Industry in Germany*, Verband Forschender Arzneimittelhersteller e.V. (German Association of Research-Based Pharmaceutical Companies) Berlin: the original source of these data is the European Federation of Pharmaceutical Industry Associations (EFPIA).

Components of Retail Pharmaceutical Prices

- In the U.S., when a prescription for an insured person is filled (avg price $70) …:
  - **Retail -** Retailer gets 20-25% (52,000 local pharmacies with more than a 1/3 in five large chains - CVS, Walgreens, Rite-Aid, Eckerd, Wal-Mart). Pharmacists cannot usually switch patients from one product to another (except for the generics) and hence are unable to exert market power against the manufacture to get any discounts --- thus pay full list price (called avg wholesale price).
  - **Wholesale -** 2-3% goes to the wholesaler who obtains drugs from manufactures, warehouses it and delivers it to the retail pharmacies (three companies, McKesson HBOC, Bergen Brunswick and Cardinal Health account for 60% of wholesaling business). Like retail pharmacies cannot switch patients from one drug to another and pay the full list price to the manufacturer

Components of Retail Pharmaceutical Prices

- In the U.S., when a prescription for an insured person is filled (avg price $70) …:
  - **Insurance companies and PBMs -** Most of the payment comes from the insurance company via the care-out managed care organizations, Pharmacy Benefit Managers (PMBs), which may get 5-15% for claims processing and negotiating with manufactures
    - PBMs are subcontractors chosen by insurance companies to develop benefit plans, administer claims and manage relationships with manufactures and retailers.
    - PBMs do not have a direct control over physicians prescribing behavior but influence it via formulary and three tiered differential copayments
    - Three Tier Drug Benefit Plan (example):

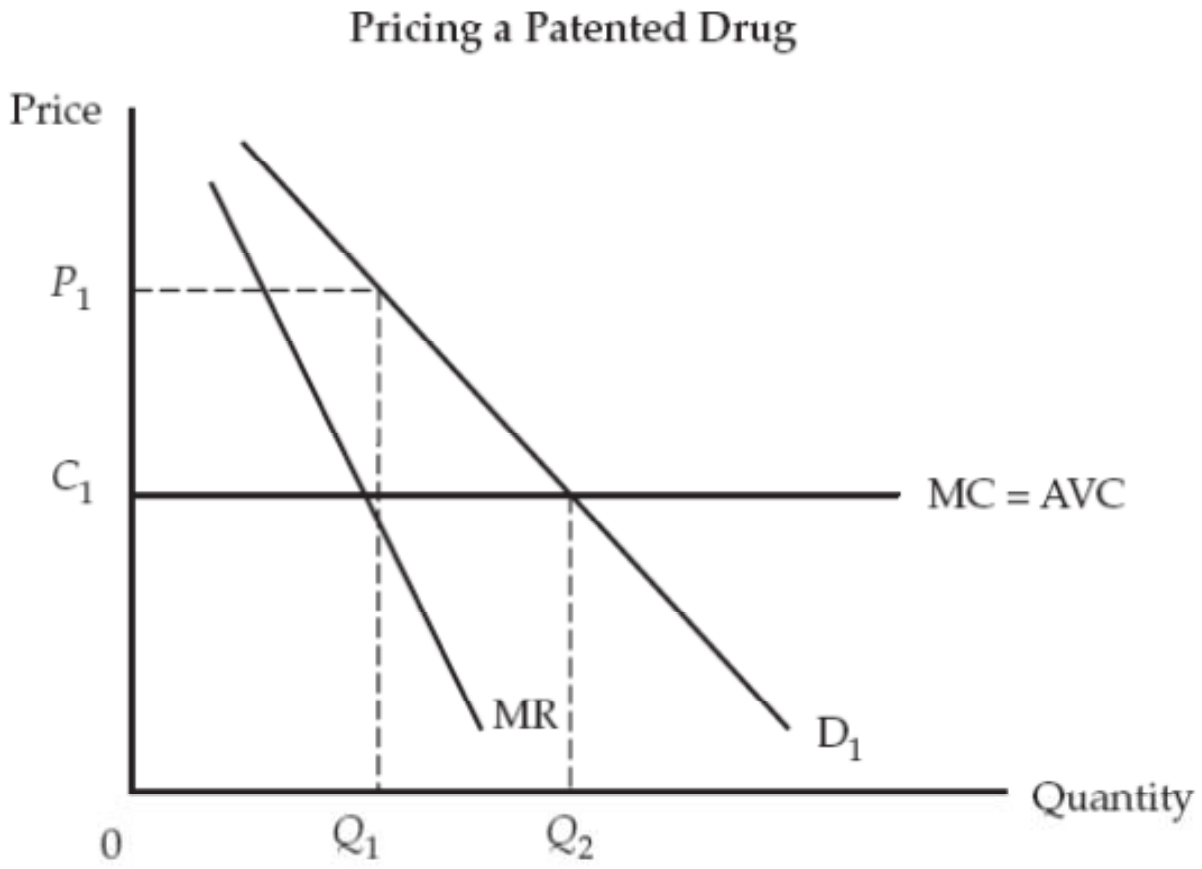
Tier	Copay	Type of Drugs
1	$2	generics, sole source
2	$10	approved formulary (drugs with no generic equivalent, drugs with small discounts)
3	$30	off-patient brands, lifestyle drugs (viagra etc).

    - PBMs consolidate the purchasing power of multiple insurance companies and employer health benefit plans and get sizable discounts from the manufactures
    - PBMs get fees from insurance companies for handling claims but also funds from manufacturer discounts
  - Three big PBMs (Express Scripts, Merck-Medco, AdvancePCS) control majority of the business and more than half of all pharmaceutical dollars flow thru PBMs.
  - **Pharmaceutical Firms -** Remainder 70-80% goes to the pharmaceutical company that manufactured the drug (generic manufactures get around 5-6%)

Drug Pricing

- Elasticity (η), or the price sensitivity, of the drug is the relevant factor when setting the price
  - Profit Maximization → MR = MC → (P-MC)/P = -1/η
  - →p(1+1/η) = MC → P/MC = η/(1+η)
- Price of branded drugs vs. the price of generics
  - The more innovative a drug and fewer the close substitutes, the greater will be the markup
  - New drugs 'prescription' and not over the counter (OTC)
  - Price of branded drugs post generic entry (increase or decrease)?

Drug Pricing

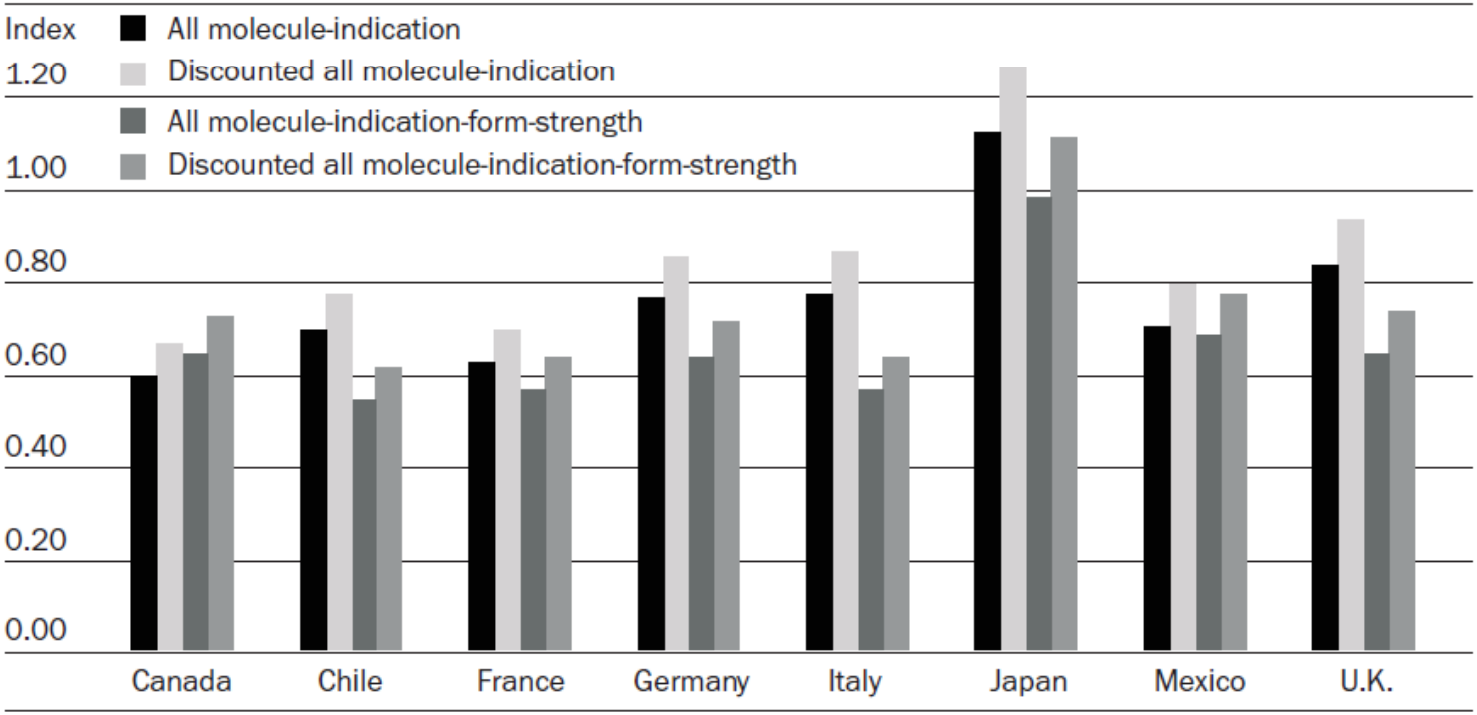


Drug Pricing

- There are significant differences internationally in the pricing of pharmaceutical products
- In the U.S., brand-name drugs tend to be higher priced than in other parts of the world
- But generic versions are often cheaper in the U.S.
- Over the counter drugs (OTC) are also generally cheaper in the U.S. than in some countries

Drug Pricing

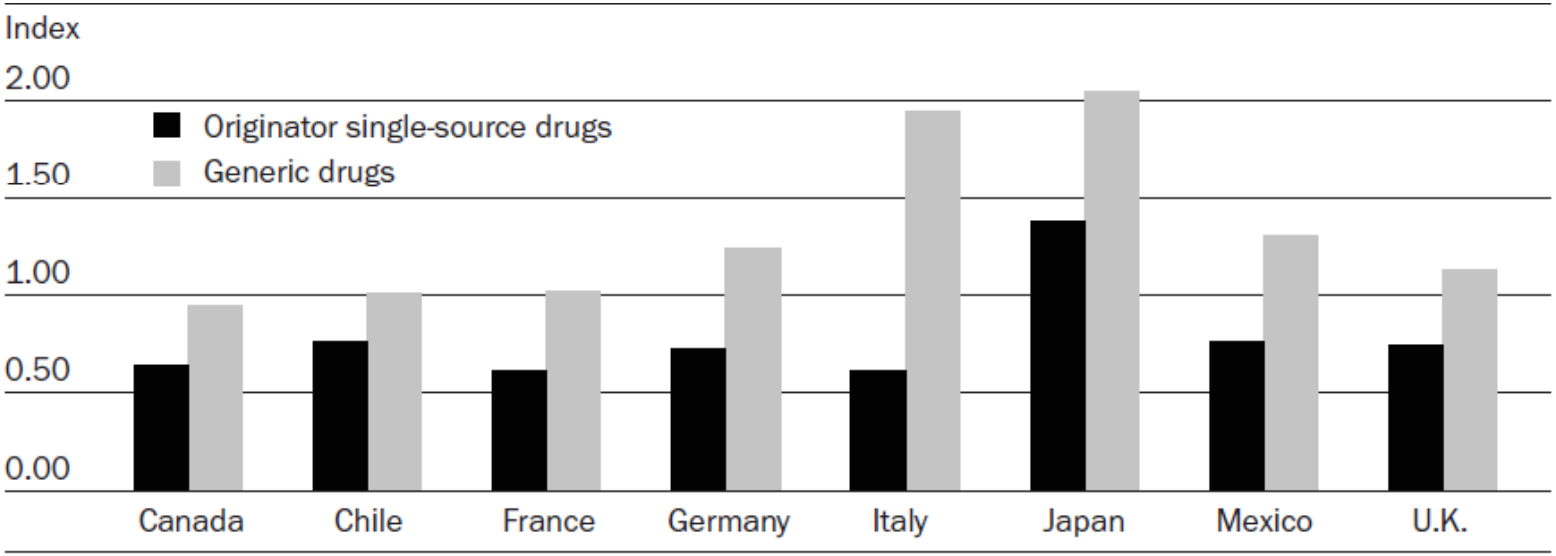
Price Indexes: Matching On Molecule-Indication Versus Molecule-Indication-Form-Strength, Without And With Adjustment For U.S. Manufacturer Discounts, Manufacturer Prices In Eight Countries Relative To U.S. Prices, 1999



SOURCE: Authors' calculations based on data from the IMS Health Midas data set, 1999.
NOTE: United States equals 1.00.

Drug Pricing

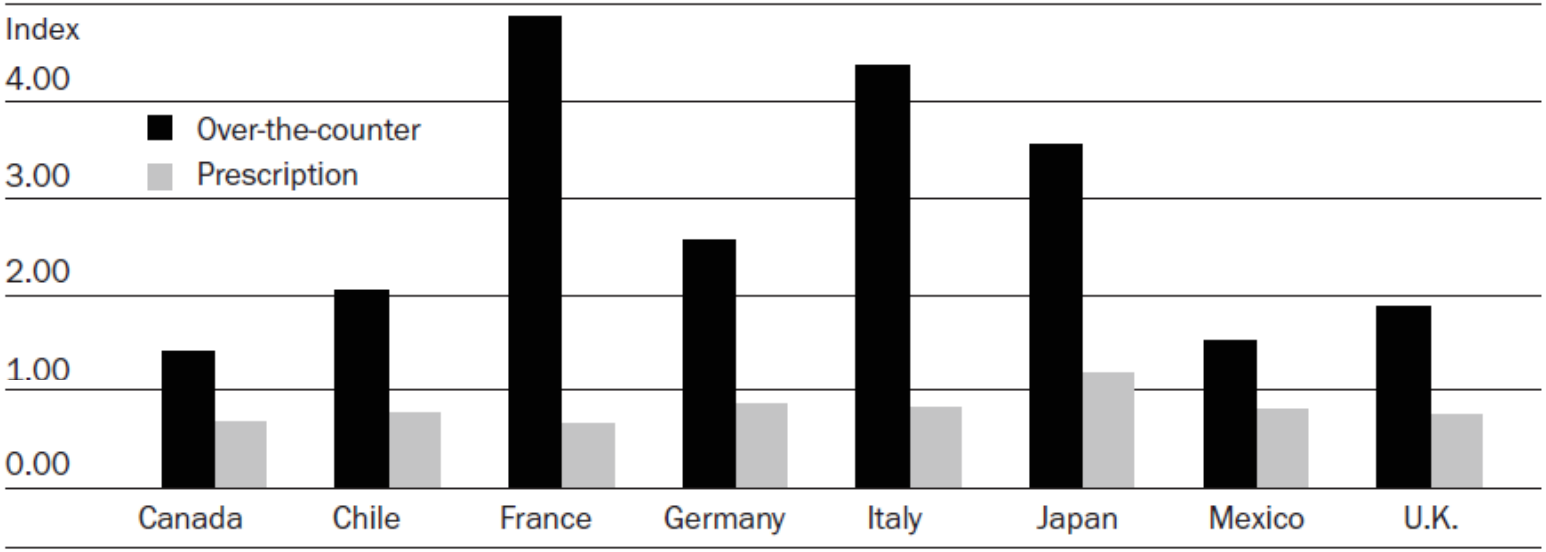
Price Indexes: On-Patent Brand-Name Drugs (Originator, Single-Source) Versus Generic Drugs, Manufacturer Prices In Eight Countries Relative To U.S. Prices, Adjusted For U.S. Discounts, 1999



SOURCE: Authors' calculations based on data from the IMS Health Midas data set, 1999.
NOTE: United States equals 1.00.

Drug Pricing

Price Indexes: Over-The-Counter Versus Prescription Drugs, Manufacturer Prices In Eight Countries Relative To U.S. Prices, Adjusted For U.S. Discounts, 1999



SOURCE: Authors' calculations based on data from the IMS Health Midas data set, 1999.
NOTE: United States equals 1.00.

Drug Pricing

- Differences in pricing reflects many factors
  - Profit maximizing behavior
  - Strategic considerations
    - Lower prices to avoid adverse publicity
    - May reflect long run profit maximizing strategies
  - Monopsony power
  - Direct price regulation
  - Availability of substitutes

Number and Size Distribution of Sellers

- Pharmaceutical companies
  - A sizeable number of large companies coexist in the drug industry
    - Brand-name pharmaceuticals, and the generic versions
  - A multitude of lesser-known, smaller firms exist
    - Generic drugs
    - Little, if any, emphasis on new drug discover

The Largest Pharmaceutical Companies by U.S. Sales, June 2007

Corporation	Total Sales (U.S. $Billions)	Market Share (percent)
Pfizer	$23.5	8.2%
GlaxoSmithKline	20.1	7.0
Merck & Co.	17.6	6.1
J&J	16.3	5.7
AstraZeneca	15.5	5.4
Amgen	14.3	5.0
Novartis	13.9	4.9
Hoffman–La Roche	12.3	4.3
Sanofi-Aventis	10.9	3.8
Lilly	10.3	3.6

Concentration Ratios for Selected Industries, 2002

NAICS Code	Industry Description	Four-Firm Ratio	Eight-Firm Ratio	Number of Firms	HHI Index
325412	Pharmaceutical Preparations	36	59	731	530
311511	Fluid Milk	46	57	315	1,013
311230	Cereal Breakfast Foods	79	91	45	2,522
312111	Soft Drinks	52	63	294	896
325611	Soap and Detergents	61	72	699	2,006
324110	Petroleum Refi ning	47	67	88	809
326211	Tires	76	83	112	1,774
327213	Glass Containers	87	96	22	2,548
327320	Ready-Mixed Concrete	11	17	2,614	57
332431	Metal Cans	69	93	82	1,518
333292	Textile Machinery	22	33	395	219
336111	Automobile	87	97	164	2,754

Number and Size Distribution of Sellers

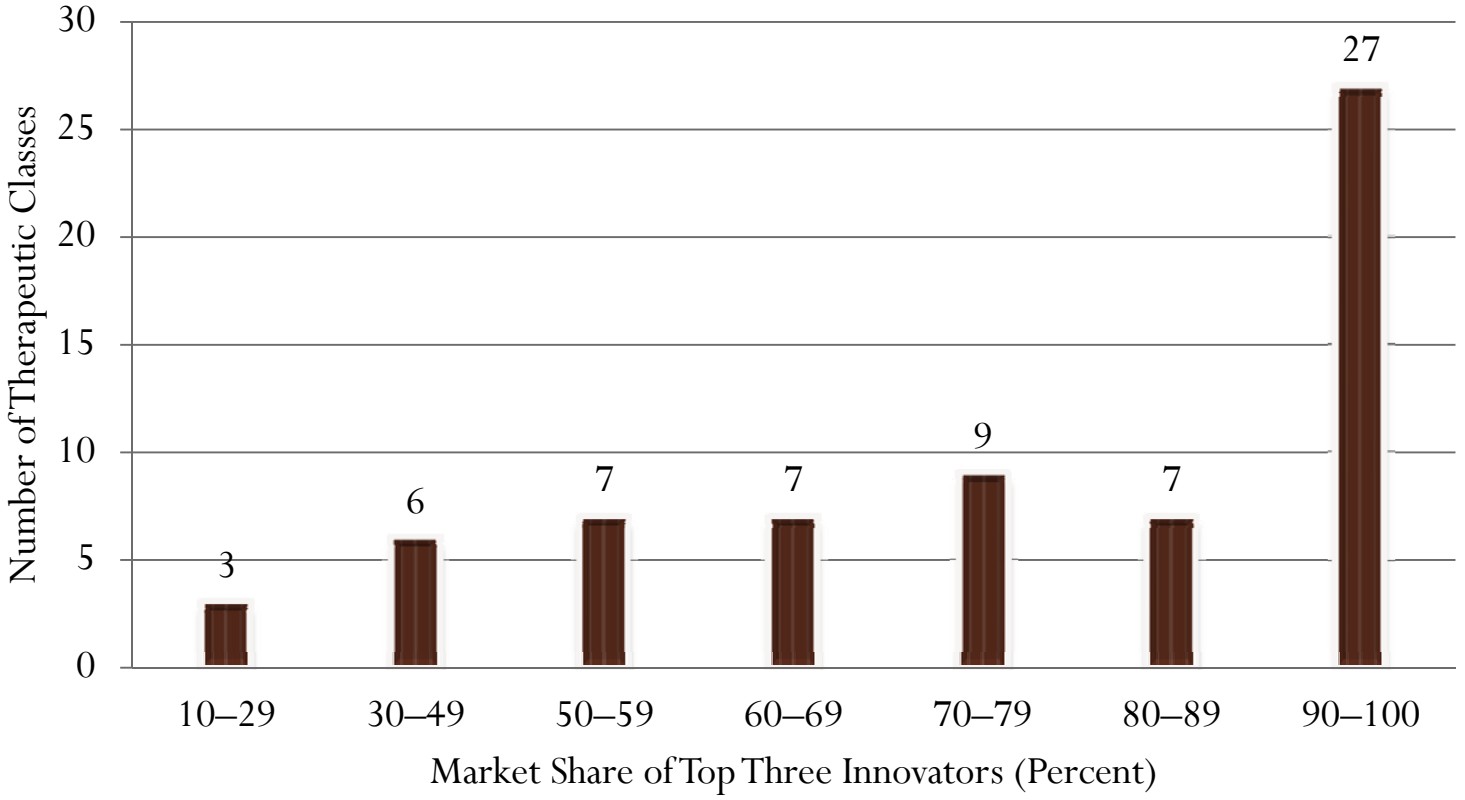
- U.S. pharmaceutical industry
  - 731 firms in 2002
    - The four largest drug firms
      - 36% of all industry output
    - The largest eight drug firms
      - 59% of all industry output
    - Herfindahl-Hirschman index (HHI) = 530
    - Assumption: relevant product market (RPM)
  - Considerable number of equally sized firms
  - Appears to be reasonably competitive from a structural perspective

Number and Size Distribution of Sellers

- Therapeutic markets
  - Narrower approach to defining RPM
  - Include only the drugs that treat common diseases or illnesses
    - Drugs are not substitutes in consumption
    - Have different intended uses
- Concentration ratios based on therapeutic markets
  - Suggest a more concentrated market environment
  - Top three drug companies
    - Less than 30% of all sales in only 3 of the 66 therapeutic markets
    - Less than 50% of sales in only 9 of the 66 therapeutic markets

Therapeutic Market	Market Share 2003
Antihistamines	99%
Anti-Rheumatics/NSAIDs	93%
Nasal Corticosteroids	89%
Gastrointestinal Disease	88%
Antihyperdipidemics	83%
Antidepressants	71%
Antivirals	70%
Antihypertensives	69%

Market Share of the Top Three Innovator Drugs in 66 Therapeutic Classes, 1994



R&D and Innovation

- Domestic R&D expenditures for members of the Pharmaceutical Research & Manufacturers of America (research-based pharmaceutical firms) rose from just over $1.5 billion in 1980 to $35.4 billion in 2007 (PhRMA, 2008).
- Patents provide protection for pharmaceutical companies so they are able to recover these R&D expenditures
- Innovating firm gains the right to be sole producer of a drug for legal maximum of 20 years
  - Preserves incentives for firms to undertake risky and costly research and development (R&D) that is socially valuable
  - Rationale: Monopoly restriction of output better than having no output at all

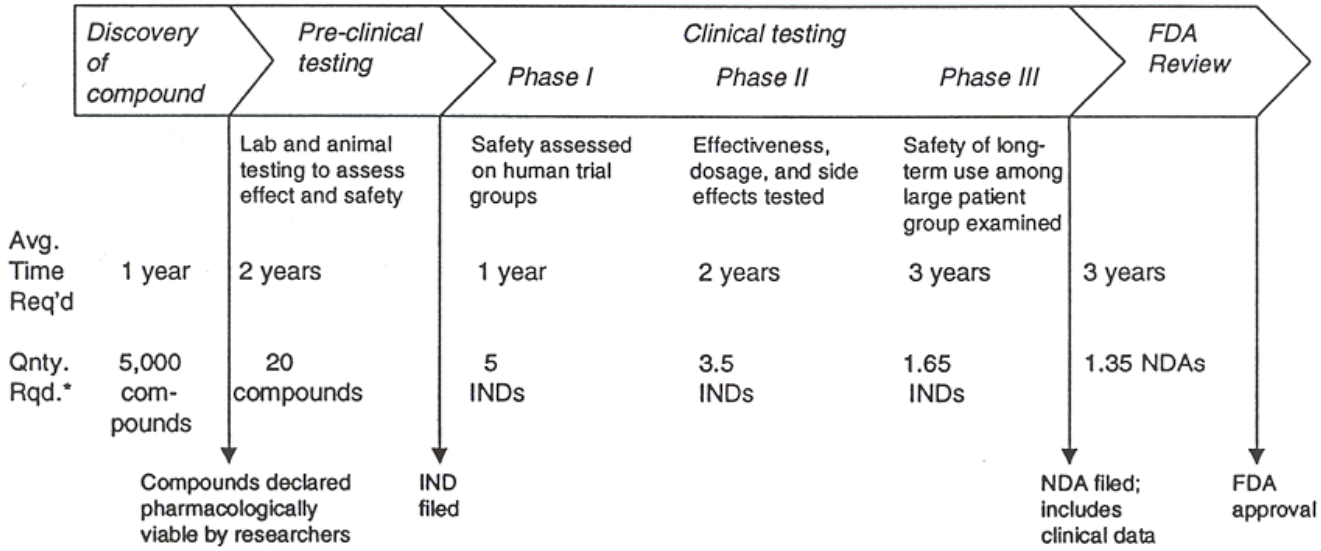
Investment Decisions

- Pharmaceutical R&D projects can be broken into 3 parts:
  - the research, testing, and review period, during which there is no revenue and large costs
  - the effective period of patent protection after product launch during which revenue will be at its highest and cost will be moderate
  - The post-patent period when revenue will diminish and costs will increase
- Net Present Value

$$NPV = \sum_{t=1}^{t=T} (R_t - C_t)/(1 + r)^t$$

Risk in Development

- Innovation is risky and time consuming
  - R&D process takes many years
  - Only a small fraction of new drug discoveries are eventually marketed
  - 75% of NCEs in Phase 1 go to Phase 2
  - 36% of NCEs in Phase 1 go to Phase 3
  - Cost of bringing a new drug to market $802 million (Harris 2001)



Risk in Development

- R&D Spending
  - DiMasi and colleagues (1991) estimated total costs, computed as capitalized expected costs and discounted at 9 percent, at $231 million in 1987 dollars per new chemical entity that was marketed
    - In a controversial update covering the late 1990s, DiMasi, Hansen, and Grabowski (2003) estimated average out-of-pocket R&D costs for new chemical entities at $403 million, in year 2000 dollars
    - This figure reaches $802 million when capitalized at 11 percent
  - Grabowski and Vernon found that a product has an effective patent life of about 9 to 13 years and a market life of about 20 years
    - Cash flows do not become positive until the third year after launch, and sales peak in the tenth or eleventh year

Risk in Development

- Mansfield (1986) found that 60 percent of pharmaceutical drugs between 1981 and 1983 would not have been developed without patent protection
- Although the effects of the patent system are small in most industries, it is critical to pharmaceutical innovation
- DiMasi et al. (2003) examined 538 investigational drugs first tested in humans between 1983-94
  - Approved for marketing (84)
  - Submitted to FDA, but not approved (9)
  - Submitted to FDA, but abandoned (5)
  - Human testing terminated < 4 years (227)
  - Human testing terminated > 4 years (172)
  - Human testing active 3/31/01 (43)

Risk in Development

- Patents
  - Significant part of patent life may be spent trying to get regulatory approval (by FDA in US, EMEA in Europe)
    - "effective" patent life = 8 years
    - Waxman-Hatch Act (1984) - benefits for both brand-name and generic companies
      - Effective life of new drug patent can be extended up to 5 years of FDA delayed market introduction
      - Fast approval process for generics: eliminated proof of safety & effectiveness
  - Monopoly power of patents is not always strong
  - Patents granted for chemical composition, not therapeutic novelty
    - Entry by me-toos
    - Tagamet & Zantac both were patented, competing in antiulcer market

Entry by ‘me-too’ drugs

- The introduction of follow-on drugs (the so called me-toos) is criticized because they reduce the profits of the innovator (and hence the incentives to engage in R&D) without necessarily offering price reductions or significant therapeutic benefits to consumers
  - Policy proposals call upon the FDA to change its approval standards and require me-too drugs to demonstrate not only efficacy relative to placebos but clinical superiority compared to existing drugs (Angell (2004), Goozner (2004), Hollis (2004))
  - Me-too drugs are typically introduced at the same price as the original branded drugs and the average effect of adding a competitor is a price reduction of about 2\% (Lu and Comanor, 1998)
  - Competition from me-toos may reduce an innovator's returns by at least as much as that from generic entry (Lichtenberg and Philipson, 2002)
  - Others argue that me-toos may provide substantial welfare gains by lowering side effects, changing the delivery mechanism or targeting a new sub-population and effectively increasing the market size (DiMasi and Paquette, 2004)

Entry by ‘me-too’ drugs

- **Ritalin:** Produced by Novartis (oldest & most known brand) consists of methylphenidate (MPH) molecule. Lasts about 3-4 hrs. Started losing market share from the mid-90s onwards.
- **Adderall, 1996:** Derived from an unsuccessful obesity drug (Obetro) and re-introduced by Shire in 1996 for approved use of ADHD. Consists of mixed dextro and levo amphetamine salts (MAS). No other producer of MAS until 2002.
- **Concerta, 2000:** Developed by Alza, distributed by Ortho-McNeil. Took an old approved molecule, methylphenidate HCL used in Ritalin (MPH) and applied a osmotic release oral system (OROS) technology for delivery. Lasts 12 hrs.
- **Adderall XR, 2001:** A year before generic entry of MAS, Shire introduced Adderall XR (patent till 2019). An extended release version of Adderall that lasts 12 hrs.

- **Metadate ER and CD:** Extended release versions of MPH molecule (by Celltech). Metadate CD is an 8 hrs. capsule (introduced in 2001) and Metadate ER is an 8 hrs. tablet.
- **Ritalin SR and LA:** Extended release versions of Ritalin (by Novartis). Ritalin LA is an 8 hrs. capsule (introduced in 2002) and Ritalin SR is an 8 hrs. tablet.
- **Focalin, 2002:** Novartis introduced a single isomer version of MPH molecule.
- **Stratera, 2002-2003:**. A non-stimulant drug (consisting of Atomoxetine) introduced by Eli Lilly.

Entry by me-toos in ADHD drugs market

Average Prices (in constant 2000 dollars) and Shares by Year (778 MSA Counties Only)

		Price ($/Gram)					Avg. Share of Revenue				
		1999	2000	2001	2002	2003	1999	2000	2001	2002	2003
(1)	Ritalin	54.0	53.3	52.8	53.6	58.2	.117	.081	.033	.016	.009
(2)	Methylin	45.3	41.9	40.0	37.9	35.4	.045	.068	.035	.022	.013
(3)	Generic MPH-IR	43.7	41.6	39.7	38.6	36.7	.289	.185	.098	.049	.026
(4a)	Ritalin SR	61.3	61.4	62.3	64.4	70.5	.047	.032	.012	.006	.003
(4b)	Ritalin LA	.	.	.	79.1	79.5	.	.	.	.006	.024
(5a)	Metadate CD	.	.	53.3	59.8	78.1	.	.	.006	.025	.024
(5b)	Metadate ER	NA	60.2	59.3	59.7	60.9	NA	.007	.007	.005	.002
(6)	Methylin ER	.	53.8	52.3	48.5	48.2	.	.004	.010	.008	.006
(7)	Generic MPH-ER	50.0	48.7	46.4	46.1	44.4	.105	.080	.034	.017	.008
(8)	Concerta	.	84.6	71.3	69.6	73.9	.	.047	.238	.298	.261
(9)	Adderall	56.5	63.1	93.7	101.7	101.3	.216	.311	.358	.114	.029
(10)	Generic MAS-IR	.	.	.	92.2	84.3	.	.	.	.084	.076
(11)	Adderall XR	.	.	112.9	116.6	125.0	.	.	.011	.202	.238
(12)	Dexedrine	49.7	53.2	59.1	66.2	67.9	.013	.010	.006	.003	.002
(13)	Dextrostat	42.1	45.9	54.5	56.0	45.2	.016	.018	.012	.005	.002
(14)	Generic DEX-IR	.	.	51.2	49.2	47.9	.	.	.003	.004	.004
(15)	Dexedrine SR	67.6	76.3	85.2	94.2	95.7	.062	.062	.045	.022	.007
(16)	Generic DEX-ER	.	.	.	84.6	83.6	.	.	.	.009	.011
(17a)	Cylert	39.6	42.0	42.6	44.2	43.9	.061	.023	.009	.004	.002
(17b)	Provigil	24.9	24.6	26.1	26.9	28.0	.022	.058	.072	.093	.094
(17c)	Generic Pemoline	32.5	31.6	33.1	31.4	29.6	.005	.015	.011	.006	.004
(17d)	Strattera	.	.	.	120.07	77.10	.	.	.	.000	.156
Total Revenue (in Millions)							688.5	836.8	1,110.3	1,438.0	1,992.7

Welfare effects of me-toos

Total CV Per County ($1000s)

	Mean	Median	Std Dev
Adderall XR	-398.54	-193.19	629.81
Concerta	-271.30	-124.20	421.08
MAS-IR*	-142.12	-67.42	219.88
Metadate CD/ER	-29.18	-12.20	46.98
Methylin ER	-26.17	-5.82	70.18

CV as Percentage of Total Expenditure Per County

	Mean	Median	Std Dev
Adderall XR	-15.60%	-15.56%	3.60%
Concerta	-11.04%	-10.86%	3.70%
MAS-IR*	-5.69%	-5.57%	1.30%
Metadate CD/ER	-1.17%	-1.14%	0.61%
Methylin ER	-0.79%	-0.54%	1.21%

CV per ADHD Child in County ($/per ADHD Child)

	Mean	Median	Std Dev
Adderall XR	-132.77	-115.67	97.29
Concerta	-88.80	-75.61	60.35
MAS-IR*	-46.15	-40.00	30.08
Metadate CD/ER	-9.54	-7.91	7.54
Methylin ER	-6.48	-3.74	9.35

* MAS-IR is generic Adderall.

Welfare effects of me-toos

- Metadate ER/CD and Methylin ER
  - Same molecule and same form as a pre-existing brandname (Ritalin SR) and several generics
  - Price increase in either Ritalin SR or the generics leads to consumers switching to these two drugs rather than each other
  - These 'branded generics' provide the easy of generics and the (perceived) quality of brands
  - Value to the consumers $9.5 and $6.5 for Metadate ER/CD and Methylin ER respectively
- Concerta
  - Unique delivery mechanism
  - Consumers switch from a broad range of drugs (across molecules) to Concerta due to price changes in other drugs
  - Price changes in Concerta leads to consumers switching to other drugs within the same molecule class
  - Several options within the molecule but not within the specific delivery mechanism.
  - Welfare gain (due to introduction) about $89 per ADHD-diagnosed child per year
- Adderall XR and generic Adderall
  - Demand for these two responds to price changes in drugs within the same molecule class
  - However, price changes in these drugs leads to consumers switching to drugs within and across the molecule class
  - Adderall XR is the extended release (ER) version of branded Adderall (only drug in ER form within the molecule class)
  - Welfare gains due to introductions about $133 and $46 respectively per ADHD-diagnosed child per year
- Not all me-toos created equal
  - Ex ante hard to judge which drug will be more valuable to consumers (consider Concerta vs Metadate CD)
  - Proposals aimed at slowing the introduction of all me-toos may not be appropriate
- Non-Entry of generic Adderall XR
  - Pay-to-delay delay between Shire and Barr
  - Generic version of Adderall XR did not enter the market till April 2009
  - Value to consumer may have been at least $46 per ADHD-diagnosed child per year

Pharmaceutical Industry Conduct

- Pricing
  - Are drug prices lower when drug firms face more intense competition
  - Are newcomers more likely to enter pharmaceutical markets when existing firms' profits are high during the post-patent period, or do post-patent barriers prevent entry
- Promotion
  - Is drug promotion informative or persuasive
  - Do the promotion expenditures of established firms impede the entry of new firms?
- Product innovation
  - Are large firms necessary for drug innovation?

Pricing Behavior

- Potential for noncompetitive pricing
  - Price drug products above the marginal costs of production and generate economic profits
    - High concentration of sales among a few firms
    - Substantial barriers to entry - therapeutic markets
  - First-mover advantages
    - Leading firms - maintain brand-name prices above costs, dominate the market
  - Promotion expenditures
    - Reinforce the habit-buying practices of many buyers, especially physicians

Pricing Behavior

- Empirical evidence, Hurwitz & Caves (1988)
  - Price differentials affect the choice between brand-name and generic products
  - Buyers are relatively insensitive to relative price changes
  - The goodwill established during the patent period extends the effective patent life of a pharmaceutical product
    - Buyers continue to pay a substantial premium after the patent has expired
  - Promotion by the leader firms helps protect market share from eroding
  - Promotion by followers tends to reduce the leader's market share

Pricing Behavior

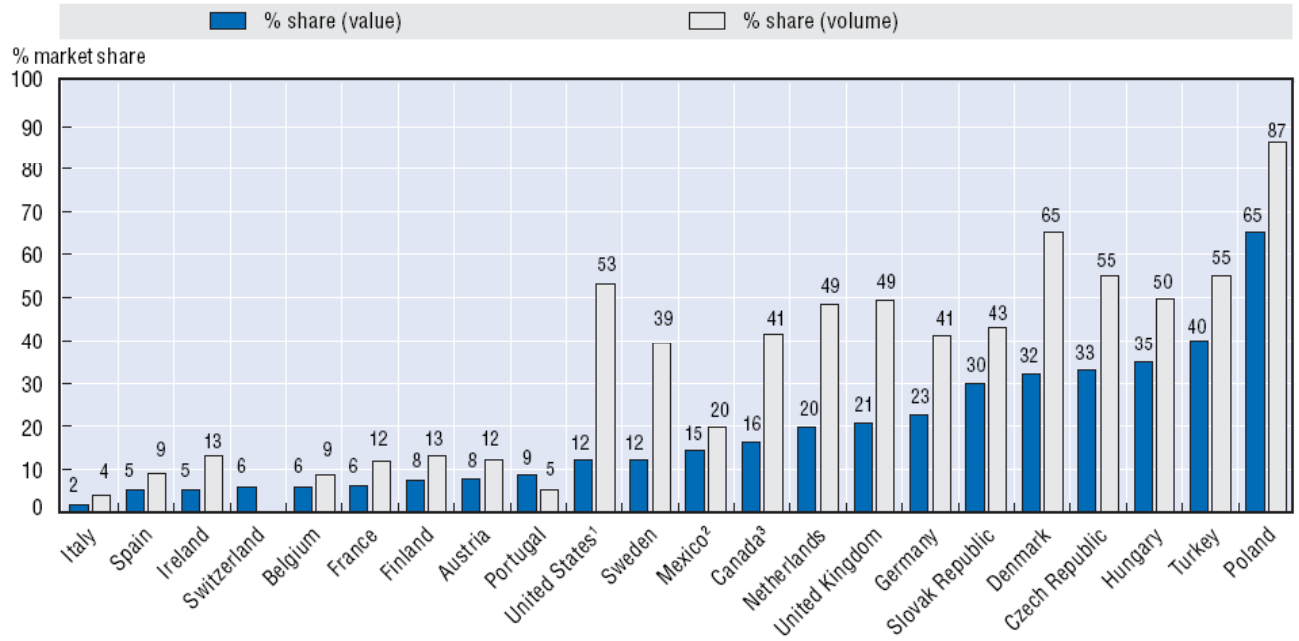
- Empirical evidence, Caves et al. (1991)
  - Leading pharmaceutical firms do not engage in limit pricing
    - The innovator's (the leading brand-name firm's) price initially rises after patent expiration
      - Up until the point where a generic competitor enters market
  - Innovator's price declines with a greater number of generic entrants
    - But by only 4.5 percent, on average

Pricing Behavior

- Empirical evidence, Caves et al. (1991)
  - Innovators' prices - more sensitive to entry during the 1980s compared to past periods
    - Reflects the growing price consciousness of pharmaceutical buyers
  - Generic producers enter markets offering prices much lower than the brand-name price
  - Generic prices - fall with further generic competitor entry
  - Generic producers - gain a relatively small market share

Market Share of Generics

Figure 2.5. **Market share of generics in terms of value and volume, 2004**



1. *Overview of North American Generic Market*, presentation by R. Milanese, President, RSM Pharmaceutical Services Inc., to the SFBC Anapharm Workshop, Malta, 19 June 2005, *www.anapharm.com/sfbc/upload/sfbc/Generateur/RobertMilanese_Overview.pdf*, accessed 7 September 2005.
2. 2002, ANAFAM (Asociación Nacional de Fabricantes de Medicamentos), *www.anafam.org.mx/quienes/historia.html*, accessed 7 September 2007 (in Spanish).
3. CGPA (2007).

Source: EGA – European Generics Manufacturers Association (2007); except Switzerland EFPIA (2006).

Pricing Behavior

- Empirical evidence
  - Both pre-patent & post-patent price competition often exist in pharmaceutical markets
  - Prices of both brand-name & generic products
    - Are lower when a greater number of substitute products are available.
  - Pioneer firms - raise the prices of their branded products upon entry
    - In response to a less elastic demand
  - The goodwill established during the patent period
    - Allows established firms to maintain a large market share despite the huge discounts offered by generic companies

Pricing Behavior

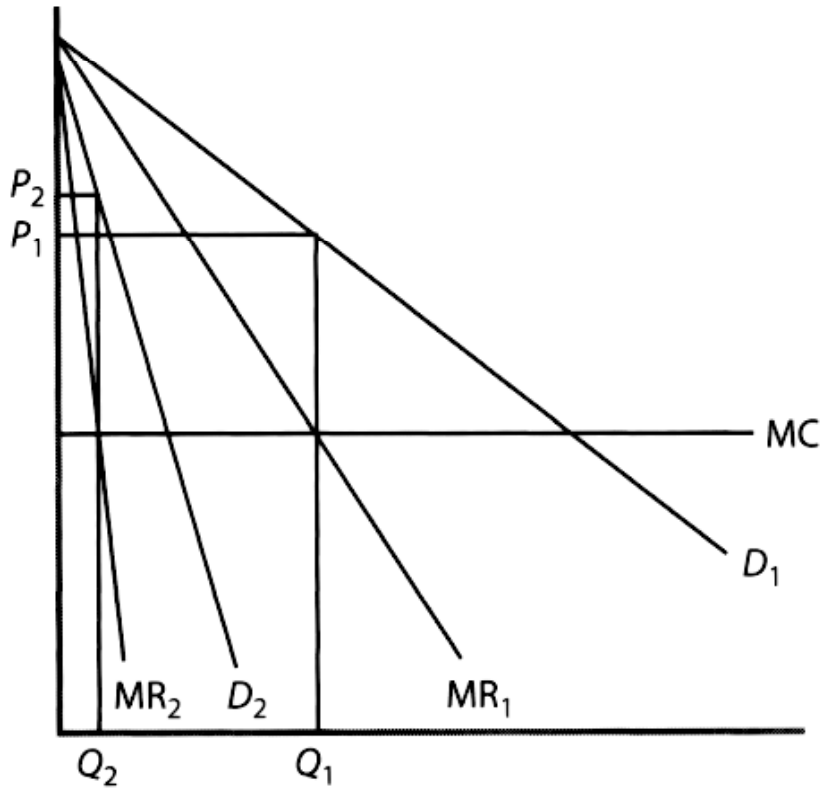
- Can the brand-name firm maintain its price once its patent expires and generics enter?
  - Average price differential between brand-name and generic firms = 127%, but brand name market share = 63.4%. (Hurwitz & Caves, 1988)
  - Branded drugs' prices ↑11% 2 years after generic entry. (Grabowski & Vernon 1992)
    - Yet brand-name drugs lost 1/2 of market share.
    - Average market price fell to 79% of pre-entry price.

Pricing Behavior

- Brand-name drugs often priced higher after they come off patent protection
  - What factors determine whether a drug price will be raised after its patent protection expires?
  - Hint: Think about what happens to the demand for the drug, including the price elasticity of demand
  - The demand for the brand-name drug decreases as generic drugs are introduced as substitutes
  - However, the demand also becomes more price-inelastic as the more loyal consumers remain
- Brand-name firms segment the market
  - Remaining customers relatively price insensitive
  - Inelastic demand curve allows them to maintain price

Pricing Behavior

- Demand for Brand-Name Drug Over Time



Promotion of Pharmaceutical Products

- Promotion expenditures
  - 20 to 30% of sales for many research-based pharmaceutical companies
  - 70% of the promotional budget - spent on personal promotion by detailers (pharmaceutical salespeople)
  - 27% - on journal advertising
  - The rest - direct-mail advertising

Promotion of Pharmaceutical Products

- Pharmaceutical promotion strategies
  - Empirical evidence, Leffler (1981), Hurwitz and Caves (1988), and Caves et al. (1991)
    - Support both the informational and persuasion effects of pharmaceutical promotion
    - Informational effect
      - Advertising intensity is greater for newer and more important pharmaceutical products
      - New entrants' promotion expenditures helped them expand their market shares
      - Increased generic competition results in less advertising by the innovator

Promotion of Pharmaceutical Products

- Pharmaceutical promotion strategies
  - Empirical evidence, Leffler (1981), Hurwitz and Caves (1988), and Caves et al. (1991)
    - Persuasion effect
      - Detailed targeting of younger physicians occurs for older products
      - Leading firms' promotion expenditures preserved their market share from new generic entrants
      - Generic firms gain relatively small shares despite their huge discounts

Promotion of Pharmaceutical Products

- May promote or impede competition depending on weather it is informative or persuasive (habit forming)
- Largely an empirical question
- Evidence mixed:
  - Leffler (1981) found evidence supporting both the informative as well as persuasive effect of promotions
  - Hurwitz and Caves (1988) – found that leading firms promotional activities preserved market share from new generic entrants (thus persuasive)
  - Caves, Whinston and Hurwitz (1991) – generic firms gain relatively small shares despite the price discounts indicating that promotion activity by innovators may lead to brand loyalty
  - All of the above somewhat indirect evidence

- More direct evidence provided by Rizzo (1999) – Directly estimated the impact of promotional activity on elasticity of demand for antihypertensive drug products
  - If promotional activity is informative then demand should become more elastic. On the other hand, if the promotional activity is persuasive and habit forming then demand should become less elastic.
  - Rizzo found that greater detailing efforts led to a lower price elasticity

Determinants of R&D Spending

- Expected marginal revenues, MR
  - Decline with respect to R&D expenditures
    - Law of diminishing marginal productivity
- Marginal or opportunity cost, MC
  - Rise or remain constant with respect to R&D spending
- Expected net profits from R&D are maximized
  - When MR = MC

Determinants of R&D Spending

- Optimal amount of R&D spending, R^*,

  $MR(R, X) = MC(R, Z)$,

  - R = investment expenditures on R&D,
  - X = vector of exogenous factors influencing the rate of return from new drug R&D,
  - Z = vector of exogenous variables influencing the marginal cost associated with new drug R&D

Determinants of R&D Spending

- Optimal amount of R&D spending, *R**,

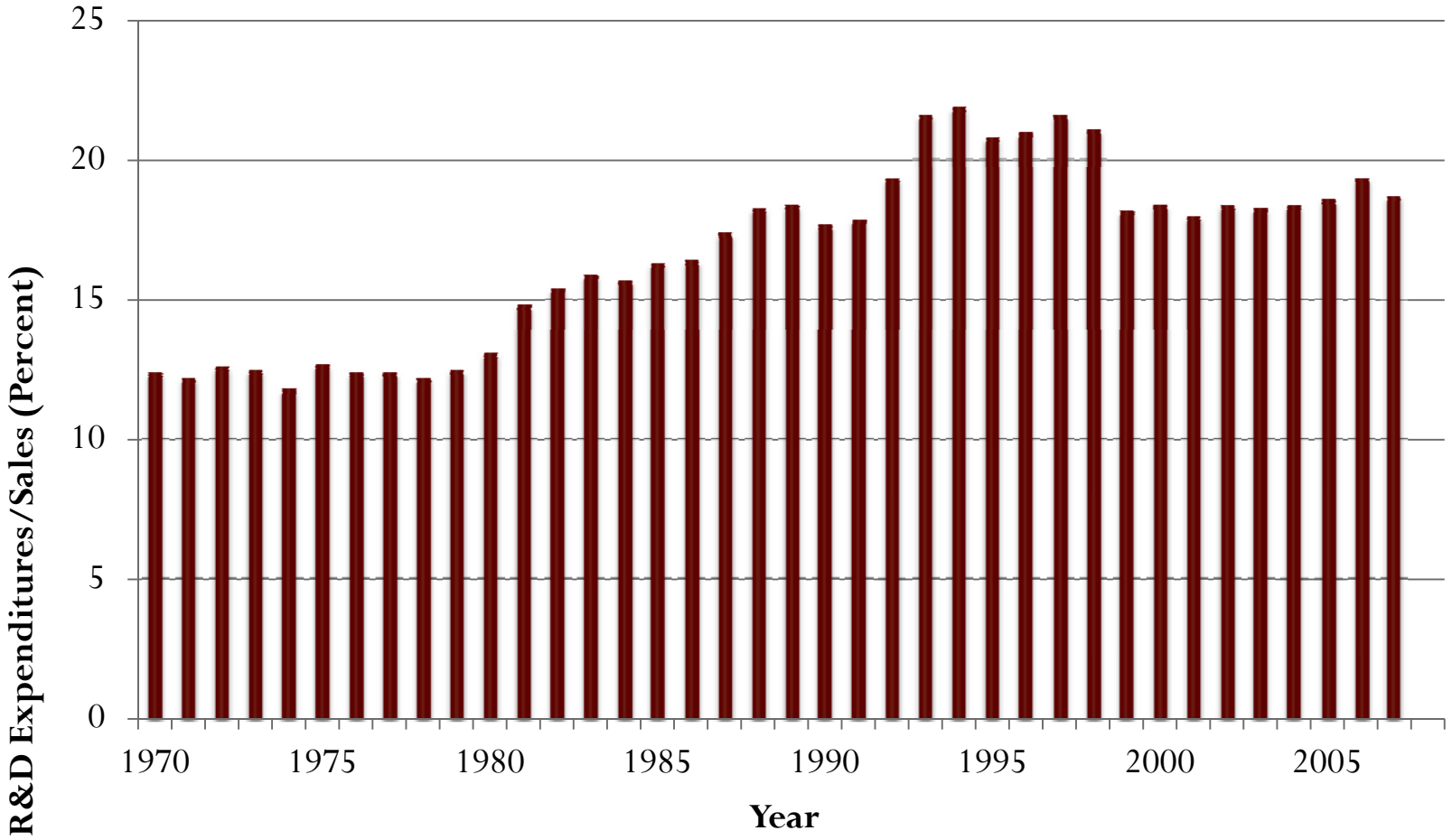
$$R^* = f(X, Z)$$

  - Variables that increase the rate of return, X, lead to increased spending on R&D
  - variables that raise the opportunity cost, Z, lead to lower R&D expenditures.

Determinants of R&D Spending

- Grabowski and Vernon (1981)
  - R&D investment spending
    - Influenced by variables affecting marginal benefit and cost
    - Increases with a greater degree of past R&D success
    - Increases with a larger cash flow margin
      - A ceiling on drug prices, by reducing cash flows, could result in a reduction in pharmaceutical R&D

R&D Intensity of Major Pharmaceutical Companies, 1970-2007



Determinants of R&D Spending

- A firm spends more on R&D if it had more success on previous R&D efforts (Grabowski and Vernon, 1981)
- Spends more if it has a larger cash-flow margin (Grabowski and Vernon, 1981)
  - Falling real drug prices in 70's and a decline in R&D spending
  - Conversely, 80's real drug prices were rising and an increase in R&D spending
  - R&D expenditures for research-based pharmaceutical companies ranged
  - 10.9% of sales in 1974 and 1978 to 21.9% of sales in 1994
  - R&D to sales ratio (R&D intensity)
  - Average 18.5% during the 2000s

Determinants of R&D Spending

- Giaccotto et al. (2005)
  - Elasticity of R&D intensity with respect to the real drug price = 0.583
- Santerre and Vernon (2006)
  - Hypothetical price control policy
    - Value of consumer surplus gains - between $176 and $767 billion by the end of 2000
    - Long-term cost - between $19.7 trillion and $21.8 trillion in terms of value of lives lost

Firm Size and Innovation

- Are large pharmaceutical firms more likely to engage in successful innovation?
  - Pre 1960's Research:
  - Large drug companies do not spend proportionately more money on R&D than smaller ones – Mansfield 1968, Grabowski 1968, Schnee 1971)
  - Post 1960's research
  - Schwartzman (1971)
    1. Research effort increases more than proportionately with the firm size
    2. Research output increases more than proportionately with research effort
    3. Larger firms discover relatively more drugs per employee than do smaller firms
  - Achs and Audretsch (1988)
    1. Large firms had 9.23 time the innovations of smaller firms
    2. But, large firms also had 19.41 times the employment of smaller drugs
    3. Thus, large firms generate only half the pharmaceutical innovations than smaller firms do on a per employee basis
    4. Small firms are about 43% more innovative than their larger counterparts

Firm Size and Innovation

- Larger firms
  - Tend to face a greater incentive to undertake successful R&D activities than smaller firms
    - Resource capability, risk absorption, and research economies
    - Greater bureaucratic red tape - stifles creativity
- Pharmaceutical innovation
  - Mixture of firm sizes
  - Smaller drug firms seem to hold a decisive advantage
  - The innovativeness of smaller firms is greatest when large firms dominate in an industry

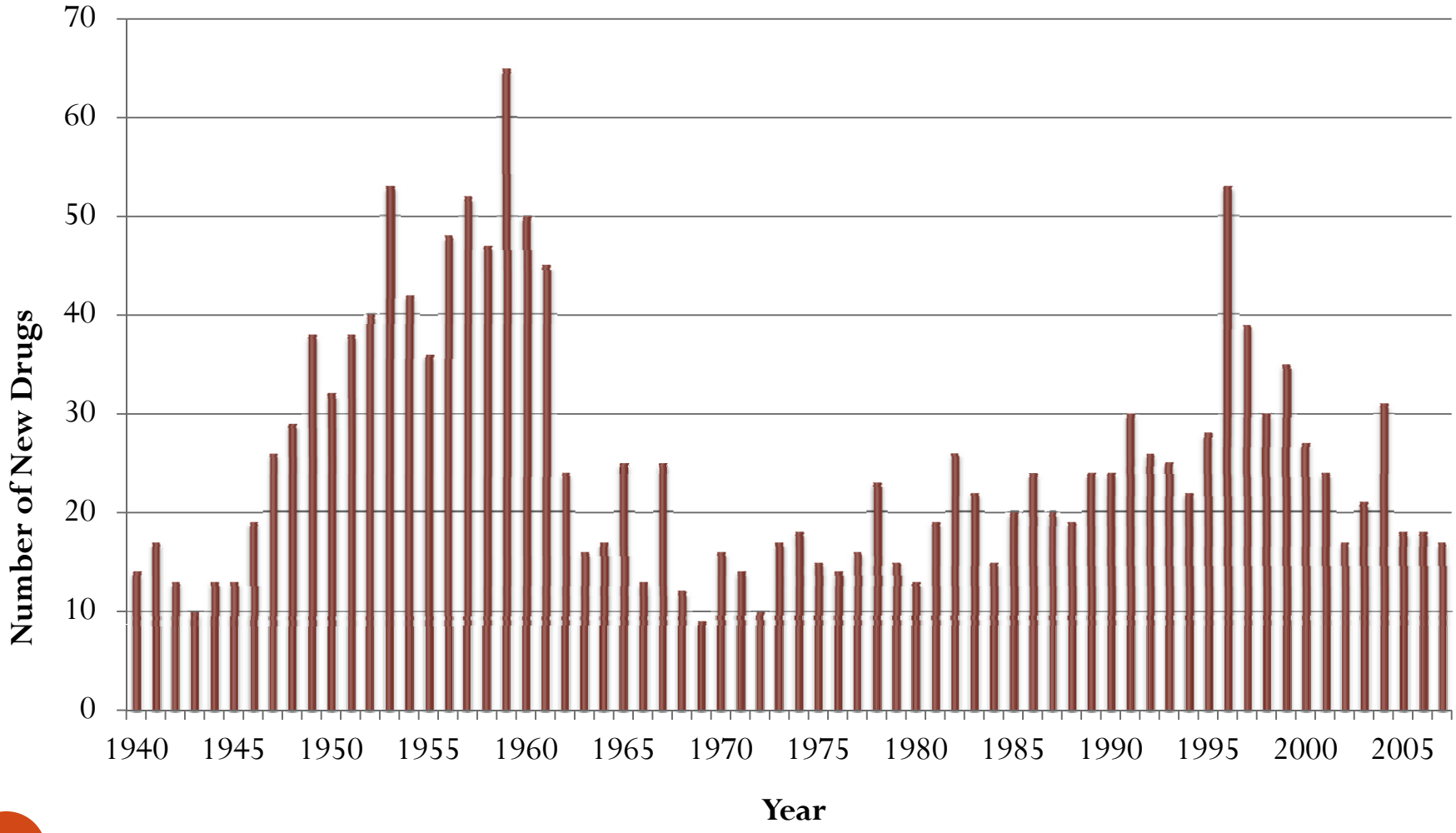
Output of New Pharmaceutical Products

- New chemical entities, NCEs
  - Improve quality of life by relieving pain
  - Significantly reduced deaths from many diseases
    - Tuberculosis, kidney infection, and hypertension.
  - Virtually eliminated diseases such as whooping cough and polio
  - Reduce the cost of treating diseases

Output of New Pharmaceutical Products

- Lichtenberg (2001)
  - Newer drugs
    - People - less likely to die & miss workdays by the end of the survey period than people who consume older drugs
    - Lowers all types of nondrug spending on medical care
      - Substantial reduction in the costs of treating a given medical condition
      - New drug offset effect
- Lichtenberg (2005)
  - New drugs have a strong positive impact on the probability of survival
    - People can expect to live one week longer each year because of new drugs
    - Produce an additional life-year at an incremental cost of about $6,750

Annual Number of New Chemical Entities, 1940–2007



Output of New Pharmaceutical Products

- Drug innovation
  - 1940s and 1950s
    - Tremendous rate at which NCEs were created and introduced
      - Reflects the birth of the modern pharmaceutical industry
  - 1960s and 1970s
    - Dramatic decline
  - 1980s and 1990s
    - Increase

Output of New Pharmaceutical Products

- Decline in drug innovations after early 1960s
  - "Depletion of research opportunities"
  - May have been the result of the 1962 amendment to the Food, Drug and Cosmetic Act
    - Significantly increased the costs of pharmaceutical innovations
      - More stringent rules concerning new drug testingand approval

Output of New Pharmaceutical Products

- Heightened innovativeness - since the beginning of the 1980s
  - Hatch-Waxman Act of 1984
    - Longer expected effective patent life for new drugs
      - Better opportunity for profits, encourages more innovation
  - Recent revolution in methods of drug discovery and development
    - Previously - molecule manipulation
    - Today - genetic engineering, monoclonal antibodies, cellular biology, and immunology

Output of New Pharmaceutical Products

- Heightened innovativeness - since the beginning of the 1980s
  - High real drug prices
    - Sizeable cash flow margins helped fund R&D expenditures
  - Prescription Drug User Fee Act (PDUFA) of 1992, and its extensions in 1997 and 2002
    - Performance goals for the FDA in terms of faster review times of NCEs.
    - FDA - collect fees from pharmaceutical companies when submitting a drug application for approval

Output of New Pharmaceutical Products

- 2000s
  - R&D intensity - above the levels observed in the 1970s and the 1980s
  - FDA approved 173 NCEs during the first seven years
  - Slowing pharmaceutical innovation in the future
    - Relatively low real-drug prices
    - Relatively dismal profit performance

Industry Profits

- **Are profits in the drug industry "too high?"**

Return on Assets for Pharmaceutical Companies in the Fortune 500		
		1997 Profits
Rank	***Company***	***as % of Assets***
4	Schering-Plough	22.2
6	Bristol-Myers Squibb	21.4
10	Merck	17.9
12	Abbott Laboratories	17.4
19	Johnson & Johnson	15.4
22	Pfizer	14.4
	500 Median	3.9

Are profits in the drug industry too high?

- Under standard accounting practices, R&D is written off as a current expense

- But R&D affects revenues for years to come
  - Rate of return on investment is calculated using an asset base that improperly excludes intangible R&D
  - Should capitalize R&D outlays & depreciate them over appropriate time periods

➡ Accounting figures overstate the rate of return on assets for drug companies

Product Innovation

- Stages of the R&D Process
  - Review the development status of a drug
  - Make decisions about continuing or abandoning the project - expected net profitability
  - Expected revenues depend on
    - Therapeutic properties of the drug, the size of the target market, and the number of substitute drugs
  - Anticipated costs depend on
    - The frequency and severity of adverse reactions to the drug and the projected additional development, marketing, distribution, and production costs

Return on Assets and Stockholder Equity for Drug and All Manufacturing Companies, Various Years

	After-Tax Return on Equity							
	1986	**1989**	**1992**	**1995**	**1997**	**2001**	**2004**	**2007**
All manufacturing	9.6%	13.5%	2.6%	16.2%	16.6%	2.0%	15.7%	15.4%
Drugs (SIC 283 or NAICS 3254)	23.1	25.3	22.3	27.0	23.2	32.1	14.6	16.3

	After-Tax Return on Assets							
	1986	**1989**	**1992**	**1995**	**1997**	**2001**	**2004**	**2007**
All manufacturing	4.2%	5.5%	0.9%	6.2%	6.6%	12.2%	7.2%	6.8%
Drugs (SIC 283 or NAICS 3254)	11.8	12.5	10.5	10.4	9.5	12.2	7.2	9.0

Profits in the Pharmaceutical Industry

- High profits
  - Patents, brand loyalty, and an inelastic demand for drugs
  - After-tax return on equity (ROE) and return on assets (ROA)
    - Profitability of drug firms is much higher than that of the manufacturing industry average
      - Pharmaceutical accounting rates of return may be biased upward due to unusually high R&D and marketing outlays
  - High R&D risks translate into high pharmaceutical returns

Profits in the Pharmaceutical Industry

- High profits
  - May be justified by the significant risk and cost of new product innovations (Grabowski and Vernon, 1990),
  - Drug prices could be reduced across the board
    - By at least 4.3%
    - Without reducing returns below the amount necessary to repay R&D Investors, (OTA, 1993)