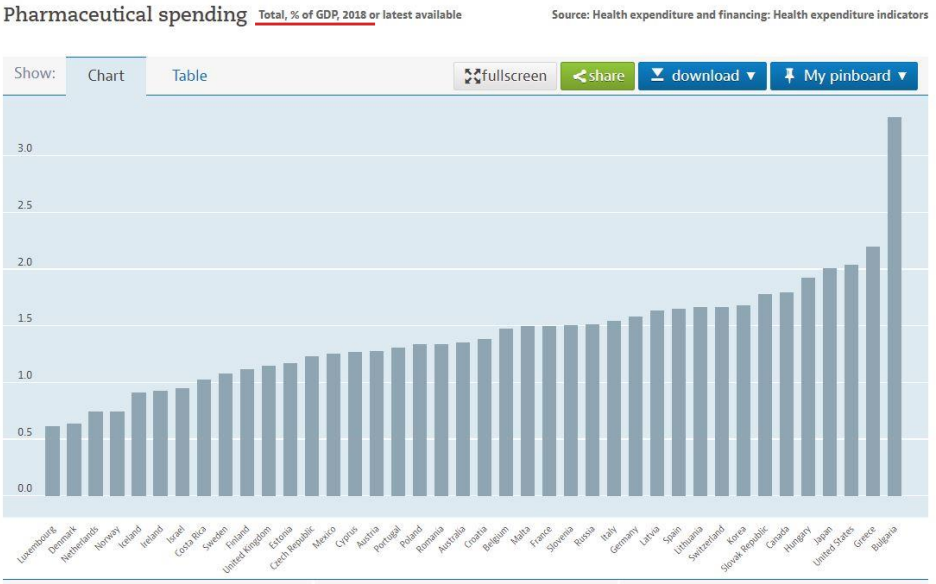
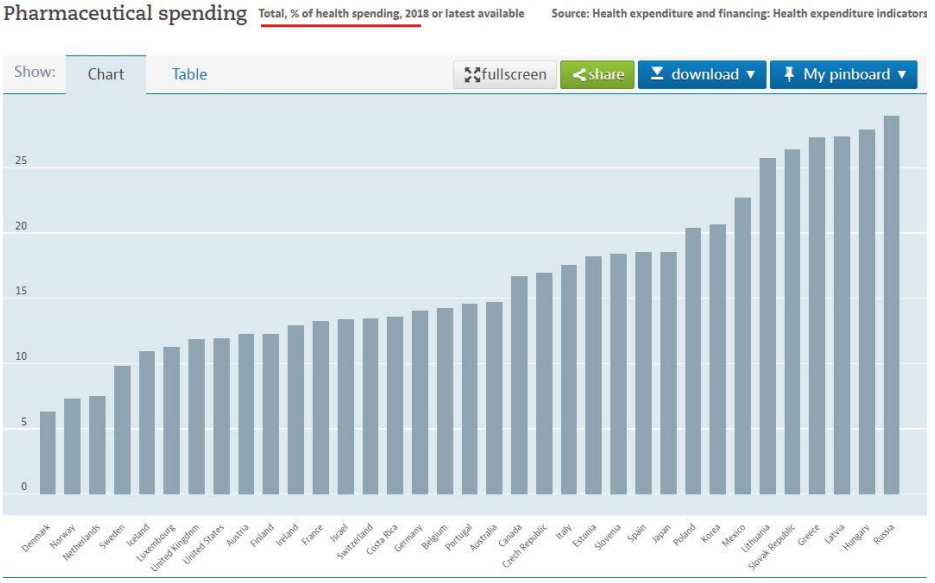
CHAPTER 12
PHARMACEUTICALS AND THE ECONOMICS OF INNOVATION

Intro

- The pharmaceutical industry got its start in 1899, when Bayer, a German chemical company, introduced a painkiller called *aspirin*
- Today, the pharmaceutical industry is **huge** and tightly **regulated**
- This industry is an ideal setting to study both the economics of **innovation** and the economics of **regulation**.



https://data.oecd.org/healthres/pharmaceutical-spending.htm



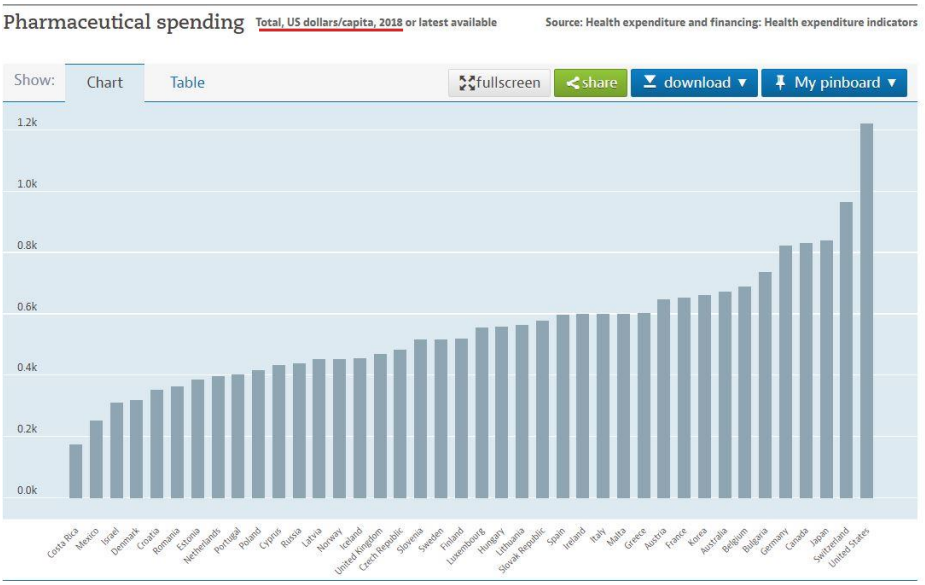
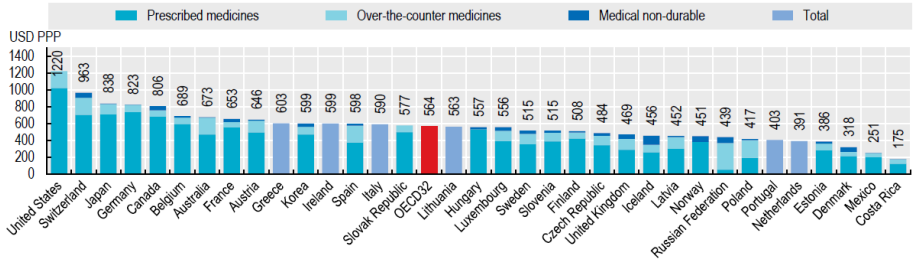


Figure 10.2. **Expenditure on retail pharmaceuticals per capita, 2017 (or nearest year)**



Source: OECD Health Statistics 2019.

StatLink https://doi.org/10.1787/888934018013

The pharmaceutical sector is **a high-technology and knowledge-intensive** industry. The industry has a two-tier structure. The largest firms account for the majority of the R&D investment in the industry and hold the majority of patents. A large number of smaller firms manufacture off-patent products or under license to a patent-holder. The pharmaceutical industry is heavily regulated. https://www.oecd.org/daf/competition/sectors/1920540.pdf

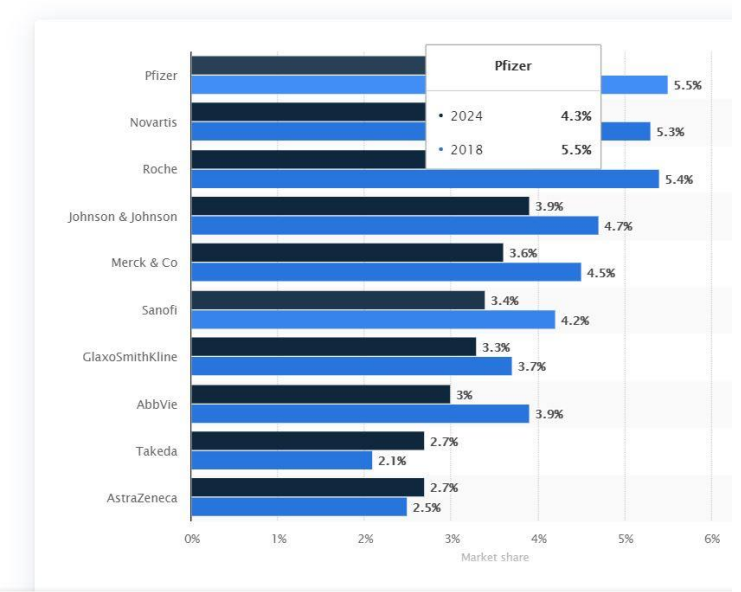
		Rx Sales*	R&D spend*	Top-selling Drugs*	
1	Pfizer NEW YORK, NEW YORK [PFIZER.COM]	$45.302	$7.962	Prevnar 13 Lyrica Ibrance	5.802 4.970 4.118
2	Roche BASEL, SWITZERLAND [ROCHE.COM]	$44.552	$9.803	Herceptin Avastin Rituxan	7.140 7.004 6.905
3	Novartis BASEL, SWITZERLAND [NOVARTIS.COM]	$43.481	$8.154	Gilenya Cosentyx Lucentis	3.341 2.837 2.046
4	Johnson & Johnson NEW BRUNSWICK, NEW JERSEY [JNJ.COM]	$38.815	$8.446	Stelara Remicade Zytiga	5.156 4.890 3.498
5	Merck & Co. KENILWORTH, NEW JERSEY [MERCK.COM]	$37.353	$7.908	Keytruda Januvia Gardasil	7.171 3.686 3.151
6	Sanofi PARIS, FRANCE [SANOFI.COM]	$35.121	$6.227	Lantus Pentacel Fluzone	4.211 2.066 2.017
7	AbbVie NORTH CHICAGO, ILLINOIS [ABBVIE.COM]	$32.067	$5.093	Humira Mavyret Imbruvica	19.936 3.438 2.968
8	GlaxoSmithKline BRENTFORD, ENGLAND [GSK.COM]	$30.645	$4.987	Triumeq Advair Tivicay	3.535 3.234 2.188
9	Amgen THOUSAND OAKS, CALIFORNIA [AMGEN.COM]	$22.533	$3.657	Enbrel Neulasta Prolia	5.014 4.475 2.291
10	Gilead Sciences FOSTER CITY, CALIFORNIA [GILEAD.COM]	$21.677	$3.897	Genvoya Truvada Epclusa	4.624 2.997 1.966

Source: EvaluatePharma® May 2019, Evaluate Ltd, www.evaluate.com

*numbers USD in billions

How the listings were compiled: 2018 Rx Sales and R&D Spend analyses were provided by life science market intelligence firm Evaluate Ltd via its EvaluatePharma® service, www.evaluate.com. *Pharm Exec* would like to thank EvaluatePharma for assisting in the development of this year's Pharma 50 listing. **PLEASE NOTE:** 2018 figures represent prescription pharmaceutical sales from the named company only, and exclude revenues from royalties, co-promotions, etc., as well as sales from non-prescription pharmaceuticals. Evaluate's Sales and R&D Spend figures represent the fiscal year that ended in 2018. For most American and European companies, that means the year ending December 31, 2018. For many Japanese companies, the fiscal year ending March 31, 2019, was used. Historic averages were used in the conversion of companies' native currency to USD.

Top 20 pharmaceutical companies worldwide bas
2018 and 2024*



The life cycle of a drug

- Find chemical compound that might treat a disease
- Then, test it on animals to show it is not toxic
- Then, test on humans in three phases
  - Phase 1: low dose to healthy individuals (~2 years)
  - Phase 2: dose to unhealthy individuals (~2 years)
  - Phase 3: test effectiveness in preventing disease or medical conditions(~3-4 years)
- Get approved for sale by FDA or similar body

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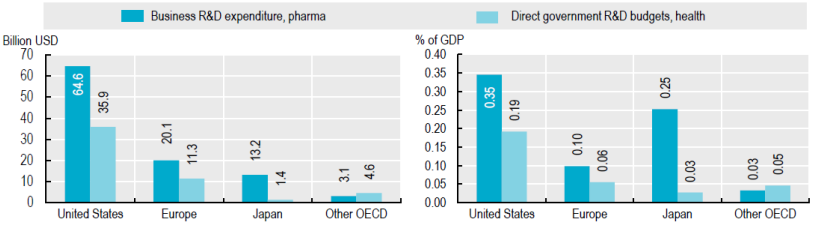
The life cycle of a drug

- Once the drug is approved for sale, the drug company has a temporary legal monopoly protected by a *patent* (20 years)
- This is the company's chance to recoup the millions of dollars spent on testing
- After that time is up, other companies can produce the same drug cheaply and profits decrease sharply

Drug development is costly

- Hard to find a promising chemical in the first place
  - Only 21.5% of drugs that enter Phase I pass to Phase III
- The whole process can cost $500 million or more to bring a drug to the point of approval

Figure 10.12. **Business enterprise expenditure for pharmaceutical R&D (BERD) and government outlays for health-related R&D (GBARD), 2016 (or nearest year)**



Source: OECD Main Science and Technology Indicators and Research and Development Statistics databases.

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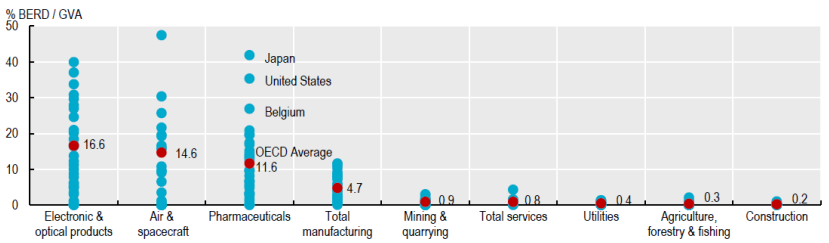
Figure 10.13. **R&D intensity by industry: business enterprise R&D expenditure as a share of gross valued added, 2016 (or nearest year)**



Source: OECD Analytical Business Enterprise R&D, Structural Analysis and System of National Accounts databases.

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How do we induce companies to make these costly investments?

- Patents create a legal monopoly and hence the opportunity for *monopoly profits*
- In practice, only the top 30% of drugs pay for themselves
- High share of R&D is financed by own resources → entry barrier

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Pharmaceuticals

Rank		Applications
1	INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM)	125
2	NOVARTIS AG	88
3	MERCK & CO	74
4	HOFFMANN-LA ROCHE LTD	58
5	UNIVERSITY OF CALIFORNIA	57
6	GLAXOSMITHKLINE	56
7	BOEHRINGER INGELHEIM PHARMA GMBH & CO. KG	54
8	BAYER AG	53
9	JOHNSON & JOHNSON	51
10	SANOFI SA	48
11	UNIVERSITY OF PENNSYLVANIA	36
12	NESTLE SA	35
13	CELGENE CORPORATION	31
14	PFIZER, INC.	30
15	UNIVERSITY OF TEXAS SYSTEM	29
16	DSM N.V.	28
17	MODERNATX, INC.	25
18	MEMORIAL SLOAN KETTERING CANCER CENTER	24
19	4D PHARMA RESEARCH LIMITED	23
19	ASTRAZENECA PLC	23
19	JOHNS HOPKINS UNIVERSITY	23
19	NOVO NORDISK AS	23
23	THE GOVERNMENT OF THE UNITED STATES OF AMERICA AS REPRESENTED BY THE SECRETARY OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES	22
24	3M COMPANY	21
24	ABBVIE INC.	21
Others		6.383
Total		7.441

PATENTS

- A patent grants its holder a **temporary monopoly** on the exploitation of an invention. The patent-holders acquires the exclusive right to prevent other parties from using, commercialising or importing the patented product or process.
- To obtain a patent, the inventor must file an application to the PTO.
- Patentability requirements:
  - Subject-matter eligibility, novelty, non-obviousness and uselfuness

PATENTS

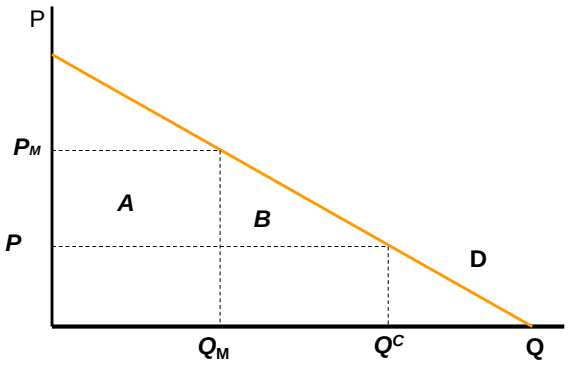
- Patent protection grants a monopoly position for twenty years but at the same time induces firms to invest in R&D.
- The traditional view is that absent patent protection firms would not invest in R&D; in fact, imitation by competitors would reduce the profits the inventor is able to appropriate.
- 'Optimal' patent protection must trade-off static vs dynamic efficiency
- Optimal design of patent along two dimensions:
  - **Patent length** and
  - patent breadth

OPTIMAL LENGTH
(Nordhaus, 1969)

Social value of **innovation** *(A+B)*
Life cycle of the product = *N years*
SW= TA-K +(N-T)(A+B)

Firm's profit: A-K
K=cost of innovation

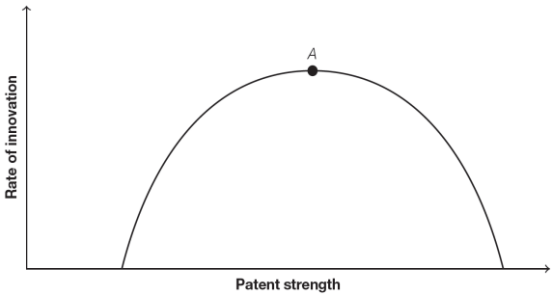
Optimal value T s.t TA-K=0 i.e.* ***T*=K/A***



OPTIMAL LENGTH
(Nordhaus, 1969)

- Optimal length is positive but finite
  - If *T* = 0, firms do not invest in R&D
  - As T increase
    - Firms invest more in R&D
    - But society must wait longer to get B.
  - If T is too long may deter subsequent innovation
    - Research and Innovation are cumulativs: they stand on the «shoulders of giants»

How strong should patents be?



- Downside of stronger patents
  - Customers have to pay monopoly prices for a longer period
  - Less incentive for further innovation by same company
  - Legal barriers to *subsequent innovation* by another company
- But if patents are too weak, no incentive to develop new drugs!

Patents in developing countries

- Low-income countries think about this tradeoff differently
  - Monopoly prices weigh more heavily on low-income populations
  - Free rider effect: if the US has patent protections, companies will develop new drugs even if there are weak patent protections in India
- Price discrimination
  - In theory, drug companies could sell their drugs for different prices in different countries
  - In practice, black-market importation makes this impossible

Price discrimination group pricing

- Consumers **differ by some observable characteristic(s)** that affect their willingness to pay (age, income, status, nationality …)
- → **Market segmentation**
  - A uniform price is charged to all consumers in a particular group – linear price
  - Different uniform prices are charged to different groups
- Firm sets higher prices in inelastic markets since demand is less responsive to prices:

$$\varepsilon_1 > \varepsilon_2 \Rightarrow p_1 < p_2$$

Welfare effects

- Profit increase
- Consumers in the market with high demand (lower demand elasticity) are worse off, since the price in this market has increased.
- Consumers in the market with low demand (higher elasticity) are better off, since price in this market has decreased

- There seems to be little evidence of price discrimination
  - No country wants to pay high price (free riding)
  - Arbitrage
  - Price controls

Where to address R&D?

- Pharma companies: choice of where to direct R&D effort is affected by potential profits.
  - Market shares
  - Price
  - Probability of success
- Innovator/Scientist responds to other incentives
  - Fame
  - Helping people
  - Research funds

Induced innovation

- **Definition**– discoveries that result when innovators change their research agenda in response to profit opportunities
- Example: changing demographics
  - As the US population aged between 1970-2000, drug companies turned their attention to drugs for the elderly (glaucoma medication, etc)

Who is harmed by induced innovation?

- Diseases that are rare (orphan diseases) or that mostly occur in developing countries (tropical diseases) receive less attention from researchers, because there is less profit to be made.
- Governments have tried to harness the power of induced innovation to fight these diseases
  - Orphan Drug Act in the US
  - Advanced purchase of yet-undiscovered vaccines for HIV, malaria, TB

Patents vs. the Pandemic (Stiglitz et al.)

- *As researchers around the world rush to develop new diagnostics and treatments for COVID-19, we must not forget that such cooperation is an exception to the rule. In the absence of public intervention, we will remain reliant for life-saving drugs and vaccines on a monopoly-driven system that favors profits over people.*

AN OUNCE OF PREVENTION (Bloom et al.)

- The current system for developing and manufacturing vaccines relies substantially on the profit motive of major multinational pharmaceutical companies
- Despite the high societal value of vaccination against diseases of epidemic potential, aspects of vaccine economics create challenges for achieving socially optimal levels of vaccine R&D, production, and uptake.
  - Global public good
  - externalities

- The Coalition for Epidemic Preparedness Innovations (CEPI) is a global partnership launched in 2017 to develop vaccines to stop future epidemics.
- CEPI, Gavi and the WHO have launched COVAX to ensure equitable access to COVID-19 vaccines and end the acute phase of the pandemic by the end of 2021.

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Covid19 Vaccine

th Economics

REGULATION OF THE PHARMACEUTICAL INDUSTRY

Ch 12 | Pharmaceuticals and the economics of innovation

Competition and Regulation Issues in the Pharmaceutical Industry

- Regulation
  - Price controls
  - Safety and efficacy
  - Prescription controls
  - Ban advertising
- Competition
  - Abuse of dominant position
  - Collusion
  - Merger Regulation

Price controls

- Price controls
  - Benefit consumers (CS)
  - Reduce spending
- In Public health systems
  - price ceilings set or negotiated by the government are the result of ***bargaining*** between government and pharma companies (monopsony or buying power vs market power)
  - Example: Italian government publishes list of maximum permissible prices for each drug
  - Example: NHS in UK sets the price at which they are willing to purchase drugs
- In US
  - Bargaining between insurance and pharma companies

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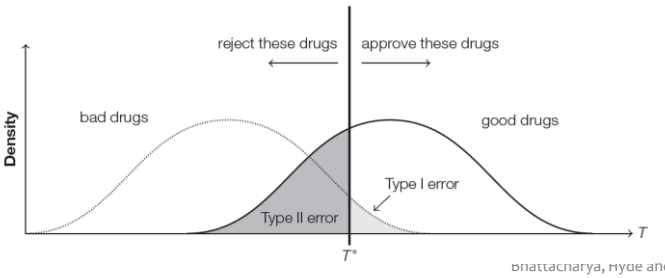
Type I and Type II errors

- The FDA has to decide how restrictive in approving new drugs
- Phase III trials do not have complete information about a drug
  - Probability distribution**s** of T
- Restrictive (high T*) vs Permissive regulations (low T*)
  - Type I error = bad drug is approved $T_B > T^*$
  - Type II error = good drug is rejected or delayed $T_G < T^*$



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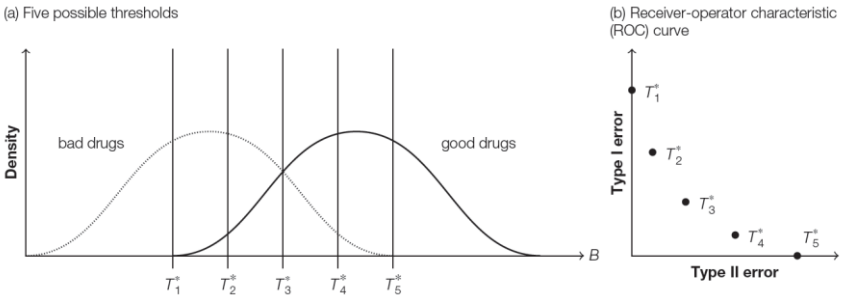
There is a tradeoff between rejecting good drugs and approving bad drugs



- Choosing T* will always lead to some error
- ROC plots the tradeoff between Type I and II errors
- Regulators balance social welfare and potential harm
  - More incentive to avoid type I errors because of media attention
  - Type II errors rarely get in the media because they are hard to catch

Other regulations

- Doctors have prescription power
  - True in most countries
  - benefit: less intentional and unintentional abuse of drugs
  - cost: time, inconvenience, expense
- Bans on direct-to-consumer (DTC) advertising
  - Bans in place in most developed countries except US
  - benefit: prevent moral hazard, reduce strain on doctor-patient relationships
  - cost: customers may not find out about new drugs that will benefit them

Conclusion

- Tradeoffs
  - Patents→ incentive for innovation vs. affordable prescriptions
  - Government price controls→ innovation vs. affordability
  - Regulation→ more new drugs vs. fewer dangerous drugs
  - Type I and II errors→ approve bad drugs vs. decline good drugs
  - Doctor prescriptions→ increase safety of drug use vs. expensive drugs