Are Drug Prices Too High?
If So, Why?

Geoffrey Joyce, PhD
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Outline

• Role of Rx drugs in rising health care spending
• Innovation versus access
• Drug development and reimbursement
• Pharmaceutical supply chain and PBMs
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Health Care Spending is Rising as a Share of Total Income in the U.S.

Wealthier Countries Spend More

Note: 1999 data for Luxembourg and Poland; 1998 data for Sweden and Turkey

It is More than Just Health Care

...It’s a Public Finance Issue
Allocation of Federal Health Care Spending by 2020

- About **one-half** to people **age 65 and older**
- About **one-quarter** to the **blind and disabled**
- About **one-quarter** to **able-bodied nonelderly** people
What Role Do Rx Drugs Play?

Rx Drugs as Share of Total Health Spending

- **Employer Plans**: 21%
- **Medicare**:
  - Part D: 17%
  - Part B: 10%
- **NHE**: 10%

[Source: USC Schaeffer]
Rx Drug Spending is Disproportionate Target

“Cost of Rx Drugs is Unsustainable” 2017 Yale report*

1. Spending on Rx drugs is increasing faster than any other component of health care spending

2. A growing number of Americans report difficulty affording their medications

*Curbing Unfair Drug Prices, Yale Law and Public Health Schools, August 2017
Net of Discounts, Price Increases Are Modest

Source: QuintilesIMS, National Sales Perspectives, Dec 2016; QuintilesIMS Institute
“Cost of Rx Drugs is Unsustainable”

Yale 2017 report

- Spending on Rx drugs is increasing faster than any other component of health care spending

- A growing number of Americans report difficulty affording their medications

Curbing Unfair Drug Prices, Yale Law and Public Health Schools, August 2017
Generic drugs now account for 90% of all prescriptions

Source: Statista
Generic drugs ensure long-term access to medications through lower prices

Express Scripts Prescription Price Index

Source: Peterson-Kaiser Health System Tracker.
Outline

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The Innovation-Access Dilemma

**Short Run**
- Society wants unfettered access to new treatments
  - Markups limit access
  - Prices should be set at cost of production

**Long Run**
- Society wants innovators to develop new treatments
  - Pharmaceutical R&D is especially risky
  - Financial incentives needed to reward risk
  - Requires IP protection: patents, market exclusivity, research subsidies

*SOURCE: Citizen Vox / Dorry Samuels*
As a result, launch prices are often controversial.
This dilemma played out dramatically with HIV

• One of the most devastating diseases globally

• New technology in the mid-1990’s revolutionized care
  – Highly active antiretroviral therapy (HAART)

• Protests over the high price of HAART

SOURCE: Ecumenical Advocacy Alliance / Paul Jeffrey
HAART had a dramatic impact on survival

Probability of Survival

Years since infection

1984

1994

2000

Most of the benefits of HAART flowed to patients

- 5% of the value flowed to manufacturers (the innovators)
- 95% of the value flows to patients (consumers)

Substantial evidence of a strong relationship between pricing power and innovation

• Evidence derives from several sources:
  – Cross-national
  – Within country natural-experiments induced by policy experiments
  – Presumptively exogenous variation in demand
Dementia kills about 1.5 million people globally — about the same as diarrhea and tuberculosis...

Leading Causes of Death Worldwide, 2015

<table>
<thead>
<tr>
<th>Cause</th>
<th>Deaths</th>
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<tbody>
<tr>
<td>Ischaemic heart disease</td>
<td>8.8 M</td>
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<tr>
<td>Stroke</td>
<td>6.2 M</td>
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<tr>
<td>Lower respiratory infections</td>
<td>3.2 M</td>
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<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>3.2 M</td>
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<tr>
<td>Trachea, bronchus, lung cancers</td>
<td>1.7 M</td>
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<tr>
<td>Diabetes mellitus</td>
<td>1.6 M</td>
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<tr>
<td>Alzheimer's and other dementias</td>
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<tr>
<td>Diarrheal diseases</td>
<td>1.4 M</td>
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<td>Tuberculosis</td>
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<tr>
<td>Road injury</td>
<td>1.3 M</td>
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<tr>
<td>Cirrhosis of the liver</td>
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<tr>
<td>Kidney diseases</td>
<td>1.1 M</td>
</tr>
<tr>
<td>HIV/AIDS</td>
<td>1.1 M</td>
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</tbody>
</table>

Source: World Health Organization
...but the distribution of the disease burden differs dramatically by income

<table>
<thead>
<tr>
<th>Lower Middle-Income Countries</th>
<th>High Income Countries</th>
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<tbody>
<tr>
<td>Ischaemic heart disease</td>
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<tr>
<td>3.3 M</td>
<td>1.7 M</td>
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<tr>
<td>Stroke</td>
<td>Stroke</td>
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<tr>
<td>2.0 M</td>
<td>758 K</td>
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<tr>
<td>Lower resp. infections</td>
<td>Alzheimer's and dementias</td>
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<td>1.5 M</td>
<td>705 K</td>
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<td>COPD</td>
<td>Lung cancers</td>
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<td>1.2 M</td>
<td>580 K</td>
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<td>Tuberculosis</td>
<td>COPD</td>
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<td>1.0 M</td>
<td>500 K</td>
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<td>Diarrhoeal diseases</td>
<td>Lower respiratory infections</td>
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<td>905 K</td>
<td>448 K</td>
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<tr>
<td>Diabetes mellitus</td>
<td>Colon and rectum cancers</td>
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<tr>
<td>707 K</td>
<td>323 K</td>
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<tr>
<td>Preterm birth complications</td>
<td>Diabetes mellitus</td>
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<td>706 K</td>
<td>265 K</td>
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<td>Cirrhosis of the liver</td>
<td>Kidney diseases</td>
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<td>594 K</td>
<td>213 K</td>
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<td>Road injury</td>
<td>Breast cancer</td>
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<tr>
<td>559 K</td>
<td>183 K</td>
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<td>Kidney diseases</td>
<td>Pancreas cancer</td>
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<td>485 K</td>
<td>175 K</td>
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<td>HIV/AIDS</td>
<td>Self-harm</td>
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<td>453 K</td>
<td>170 K</td>
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<tr>
<td>Birth asphyxia and trauma</td>
<td>Cirrhosis of the liver</td>
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<tr>
<td>414 K</td>
<td>164 K</td>
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</table>

Source: World Health Organization
More R&D for Alzheimer’s than TB

Treatments Under Development, 2017

The 1982 US Orphan Drug Act increased development for rare diseases

Source: W. Yin, *Journal of Health Economics*, 2008 (Figure 1).
Part D increased development in classes favoring Medicare patients

Top U.S. Therapeutic Classes, by Sales ($ Billion, 2016)

- HIV antivirals: 25
- Antivirals (ex-HIV): 33
- Mental health: 37
- Autoimmune: 45
- Antibiotics and vaccines: 54
- Respiratory: 54
- Antidiabetes: 66
- Pain: 68
- Cardiovascular: 71
- Oncologics: 75

Source: Statista
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The costs of drug development have increased over time

Average Cost to Develop One New Approved Drug—Including the Cost of Failures
(in Constant 2013 Dollars)

KEY DRIVERS of increasing R&D costs:
• increased clinical trial complexity
• larger clinical trial sizes
• greater focus on targeting chronic and degenerative diseases
• higher failure rates for drugs tested in earlier-phase clinical studies

*$Previous research by the same author estimated the average R&D costs in the early 2000s at $1.2 billion in constant 2000 dollars (see DiMasi JA, Grabowski HG. The cost of biopharmaceutical R&D: is biotech different? Managerial Decis Economics. 2007;28:469-479). That estimate is based on the same underlying survey as the author’s estimates for the 1990s to early 2000s reported here ($800 million in constant 2000 dollars) but is updated for changes in the cost of capital.

Source: DiMasi JA, et al. 21

USC Schaeffer
Expect 30-35 new molecules per year

Global Launches of New Molecular Entities

Source: IMS Institute for Healthcare Informatics, October 2013
The R&D problem

The technology sector follows Moore’s Law
- Doubling # transistors on an integrated circuit every year

Opposite trend in pharmaceutical R&D
- R&D Efficiency = \( \frac{\text{No of new drugs}}{\$ \text{ billion spent on R&D}} \)
- Steady decline in R&D efficiency over the past 5 decades
US Trends in R&D efficiency (inflation-adjusted)

NOTES: based on a figure that originally appeared in a Bernstein Research report (The Long View — R&D productivity; 30 Sep 2010).
Why is R&D efficiency declining?

1. The bar keeps rising
   - Yesterday’s blockbuster is today’s generic
   - Growing inventory of approved medicines increases clinical threshold needed to obtain approval

Consequences:
   - Reduces the value of undiscovered drugs
     - Deters R&D in some areas
     - Crowds R&D in hard to treat diseases
Why is R&D efficiency declining?

2. Cautious regulators

- Regulator is more risk tolerant when few good treatment options exist
  - e.g. HIV drugs in 1980’s
- Progress raises evidentiary hurdles for approval, adoption and reimbursement
  - Increases clinical trial size
  - Greater concern about adverse events
- Bottom line: regulators are more cautious
Advances in basic and regulatory science have not compensated for R&D productivity declines

- Enormous progress in basic research and screening methods
- Increased efforts by regulators to guide emerging technologies
- Yet, the probability that a small-molecule drug successfully completes clinical trials is unchanged over past 50 years

Industry response: Mergers, licensing, R&D reductions

Top 20 pharmaceutical companies by market capitalization in 1995

- Schering-Plough
  - Wyeth
  - Pharmacia
  - Warner-Lambert
  - Wellcome
  - SmithKline Beecham
  - Astra AB

- Astellas
- Daiichi Sankyo

Acquired

- GlaxoSmithKline
- Merck & Co.
- Pfizer
- AstraZeneca
- Bayer
- Takeda
- Roche

- Amgen
- Bristol-Myers Squibb
- Johnson & Johnson
- Eli Lilly

Dropped out of top 20

Top 20 survivors¹

¹ Still among the top 20 pharmaceutical companies by market capitalization as of Dec 31, 2012.

Source: Dealogic; TPSi; McKinsey analysis
R&D responses also reflect uncertain reimbursement

- Spending per patient for a drug is rising
- Median number of patients treated is falling
- Can high nominal prices compensate for smaller patient populations?
Example of Patents and Market Exclusivity

<table>
<thead>
<tr>
<th>2000</th>
<th>2004</th>
<th>2010</th>
<th>2012</th>
<th>2025</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-year patent filed on a drug</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

Hatch-Waxman Act: extends patent for one-half of time drug was in clinical trials (3 years) + all time time drug was under FDA review (2 years), up to max of 5 years.

**Effective patent life:**

- 8 years remaining on original patent +
- 5 year extension due to Hatch-Waxman +
- 0.5 year pediatric extension for conducting pediatric dosing studies.

**Note**: Generic manufacturers need to prove their drug is bio-equivalent to the drug losing patent protection.
With Lack of Federal Legislation, States Taking the Lead in Constraining Rx Prices

• In 2017, 80+ Rx pricing bills proposed in 30+ states
  – Legislation passed in MD, NY and NV
  – Several states considered bills to lower drug prices

• Targeting excessive pricing of generic and brand drugs
  – Prohibiting unfair launch prices
  – Capping annual price increases

• Mandating the release of pricing information
  – Development, manufacturing, and marketing costs on each drug
Are these the Right Policies?

• Ensuring patient access is a worthy goal
  – Out-of-pocket maximums and/or annual caps protect highest users

• Targeting Rx drugs with price controls is misplaced
  – Many problems with our current system
  – Setting long-term policies based on short-term price controls will not effectively address them
  – Lessen the incentives for drug innovation

• Instead: restructure current third party payer system
Outline

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The Role of the Supply Chain in High Drug Prices

Administer prescription drug insurance benefits

• Real time claims adjudication
• Manage a network of pharmacies
• Negotiate rebates for the first time
• Administer prescription drug cards
• Offer limited mail service fulfillment
• Interventions
  • Drug interactions
  • Limited DUR

PBM Humble Beginnings – 1980s
PBM Growth & Evolution – 1990s

- **Plan administration expansion**
  - HMO/Managed Care/Self-funded
  - Expansion of rebates and formulary design
  - Aggressive mail order growth
  - More clinical services
    - DUR/Retrospective DUR/Interventions/Disease Management/Drug interactions
  - More competitive rebates
  - Expansion of data offerings

- **Pharmaceutical manufacturers buy PBMs**
  - Establish greater presence in managed care
  - Secure formulary status for their products
PBM Growth & Evolution — 2000s

- PBM began to offer enhanced clinical services
  - Enhanced DUR review; prior authorization
  - Clinical account management
  - Increasingly sophisticated data driven strategies
    - Consumer behavior modifications
    - Provider data
    - Enhanced member level data
- PBM consolidation
  - Negotiate better discounts and rebates
  - Lower reimbursement for network pharmacies
  - Lower Rx benefit costs for clients
Three PBMs Control 70% - 75% of the Market

- Provide key services:
  - Administration
  - Claims processing
  - Utilization review

- Negotiate directly with manufacturers:
  - Prices
  - Formulary placement

- Leverage market power (DOJ allows merger of #’s 1 & 2 in the industry)
Lack of Transparency Allows PBMs to Make Money in a Variety of Ways

1. Rebates from manufacturers
   - Formulary placement/exclusions drive utilization
   - Increasing size/awareness of rebates led to new contracts
     - “Pass through” or guarantee % of rebate to plan sponsor
   - PBMs responded by adding an assortment of “administrative fees”

2. Spread Pricing
   - Buy low, sell high
     - Reimburse pharmacy $X
     - Bill plan sponsor ($X + $Y)
Lack of Transparency Allows PBMs to Make Money in a Variety of Ways

3. Maximum Allowable Cost (MAC) Pricing

- Each PBM sets the MAC price or upper limit it will pay for generic and multisource drugs,
  - e.g. $15 for a 30-day supply of 20mg atorvastatin
- No standard methodology for deriving MAC list
- Plan sponsors often unaware of MAC price
  - PBMHs create multiple MACs for different entities
    - And can change them at will
- Used to create a spread between what they charge a plan and amount they reimburse the pharmacy
How Much Does the Supply Chain Add to the Price of a Drug?

• **5.8x**: Average price difference between what a generic manufacturer receives per pill and what the health plan charges the same manufacturer when its employees use the drug

• Another example:

<table>
<thead>
<tr>
<th>Drug generic (brand)</th>
<th>Strength / Qty</th>
<th>Price charged to employer</th>
<th>Online Price (uninsured consumer)</th>
</tr>
</thead>
<tbody>
<tr>
<td>atorvastatin (Lipitor)</td>
<td>40mg / 90</td>
<td>$153.73</td>
<td>$17.89(^a) - $66.34(^b)</td>
</tr>
<tr>
<td>rosvuvastatin (Crestor)</td>
<td>40mg / 90</td>
<td>$158.42</td>
<td>$24.66(^c) - $257.52(^d)</td>
</tr>
</tbody>
</table>

Notes: \(^a\) Ralphs; \(^b\) Walmart; \(^c\) Costco; \(^d\) Walgreens. Online prices from GoodRx on 6/12/18.
Consolidation & Conflict of Interest
Raise Drug Prices

• Consolidation
  • Three largest PBMs dominate the market
  • Hard for plans to assess PBM performance
  • Strong “penalties” for deviating from national formulary

• Conflict of interest
  • Vertical integration
    • United Healthcare owns Optum
    • Cigna merging with Express Scripts
    • CVS Caremark owns large retail pharmacy chain
  • Recent investigation of CVS Caremark in Ohio
    • Reimbursing CVS pharmacies more than independents
Not Surprisingly, PBMs are Highly Profitable

• In 2017, Express Scripts reported gross profits of $8.76 billion
  – Don’t take possession of the drug (excl mail-order)
  – Bear little risk
  – EBITDA (earnings before interest, taxes, depreciation and amortization) ≈ 85% of gross profits, or about $7 billion in 2017.
  – Substantially higher (risk-adjusted) returns than other entities, i.e. manufacturers, pharmacies, wholesalers, insurers
  – Reflected in their stock prices
# National Formularies of Largest PBMs

<table>
<thead>
<tr>
<th>GLP1 Ago</th>
<th>Brand Name</th>
<th>Generic Name</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
<th>2018</th>
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<td>Victoza</td>
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Does Greater Transparency Result in Lower Drug Prices?

• Large PBMs claim they obtain larger discounts from manufacturers
  • “It’s a black box, but still cheaper to go with us”
• But “transparent” contracts or self-managed plans have led to substantial savings
  • U. Michigan saved $55 million in 6 years;
  • NJ projects savings of $559 million over 6 years
• Exchange plans (ACA) and Medicare Part D require PBMs to report all discounts/rebates and price concessions
  • How much is passed through to the plan
  • Difference between amount paid by plan vs. pharmacy
**Employee Retirement Income Security Act (ERISA)**

- ERISA is a federal law that sets minimum standards for most voluntarily established pension and health plans
  - Provides protection for individuals in these plans
- Requires plans to provide participants with important information about plan features and funding
  - Plans must act in the interest of the participants
- What would happen if PBMs were subject to ERISA?
  - No spread pricing
  - Full rebate pass-through;
  - No clawbacks or favoring brands over generics
Value-based pricing is Increasing

- Portfolio pricing
- Capitated payments or "drug licenses"
- Care-Management Solutions
- Bundling of drugs and services
- Money-back guarantees or "drug warranties"
- Adherence-based pricing

USC Schaeffer
President Eisenhower’s Heart Attacks

Ike suffered from acute coronary syndrome (ACS)

- Frequently results in one or more heart attacks (AMIs) of increasing severity

Today, ACS patients are treated with a variety of drugs: aspirin, beta-blockers, ace-inhibitors, statins, and clopidogrel

- Post-AMI patients face just under 50% risk of future heart attacks

In 1955, recommended treatment for post-AMI patients was bedrest

- With this treatment, risk of future heart attacks is 100%!