Pharmaceutical Pricing

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Disclosures

• No one in our Division has personal financial relationships with any pharmaceutical company

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MOOC

Week 1: The FDA—its history, public health role, and how it makes the rules affecting the US prescription drug market (special guest: Peggy Hamburg)

Week 2: The process of discovering, testing, and approving innovative drugs (special feature: mock Advisory Committee)

Week 3: The cost of prescription drugs, including the factors affecting a drug’s market exclusivity period and the availability and use of inexpensive generic drugs (special guest: David Mitchell)

Week 4: The promotion of prescription drugs by pharmaceutical manufacturers to physicians (e.g., via sales representatives) and patients (e.g., via direct-to-consumer advertising) (special guests: Steve Woloshin and Lisa Schwartz; Leeza Osipenko, NICE; Shahram Ahari)

Week 5: Post-approval evaluation of prescription drugs (special guests: Geral Dal Pan, FDA; Richard Platt, Sentinel)

Week 6: Current debates over the scope of FDA regulation: Dietary supplements; stem cell therapies; FDA regulation of emerging technologies (special guest: Dan Carpenter)

Click here to view trailer
Policy dilemma

• Drugs are among the most effective and cost-effective interventions in medicine

• Drug industry plays important role in bringing products forward, which can require substantial resources

HOWEVER…

• Drug prices in the US continue to rise, which can make breakthroughs unaffordable for many of our patients
  – Bad clinical consequences
  – Driver of US health care spending
Prescription Drug Spending in the US

- Sales: $456 billion in 2017
  - 22% of health care spending (IMS)
  - 19% of Medicare spending (MEDPAC)
  - 19% of employer-based insurance benefits (Kaiser)

- International per capita comparisons
  - US: $858; avg 19 industrialized countries: $400

Schumock et al, AJHP 2018; Kesselheim et al, JAMA 2017
Brand-Name Drugs

• 10% prescriptions, 72% of spending
• 164% increase in price from 2008-2015 of most commonly used brand-name drugs
  – 12% increase in CPI, 28% increase in aggregate health care spending
Average Annual Brand Name Drug Prices Continue to Grow Substantially Faster than General Inflation in 2017

**Note:** Calculations of the average annual brand name drug price change include the 267 drug products most widely used by older Americans (see Appendix A).

Prepared by the AARP Public Policy Institute and the PRIME Institute, University of Minnesota, based on data from Truven Health MarketScan® Research Databases and MediSpan Price Rx Pro®.
Monthly and Median Costs of Cancer Drugs at the Time of FDA Approval
1965 - 2015

Source: Peter B. Bach, MD, Memorial Sloan-Kettering Cancer Center
Not limited to brand-name drugs

- Among >21,000 generic products (2008-2015), 400 (2%) increased more than 1,000%

Source: Truven Health Analytics

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Clinical consequences

- More patients have coverage due to Medicare drug benefit and ACA, cost-containment strategies have shifted drug expenses onto patients’ shoulders
  - Medicaid programs facing higher drug costs have had to cut back on other services or have tightened eligibility requirements
- 25% of patients in 2016 reported that they or another family member did not fill a prescription in the last year due to cost
- Patients prescribed a costly branded product rather than a more affordable generic alternative adhere less well, and have worse health outcomes

Explanations

1. “High prices drive innovation”
   - ... but innovation that leads to transformative new drug products is often performed in academic institutions and supported by public investment such as the National Institutes of Health
   - ... but proportion of large pharmaceutical company revenues that goes to R&D is 10-15%

Kesselheim et al., *Health Affairs*, 2015
Sales and R&D expenditures of 10 largest drug manufacturers in 2014

<table>
<thead>
<tr>
<th>Ranking</th>
<th>Company</th>
<th>Total Sales $ Millions</th>
<th>Research and Development $ Millions</th>
<th>Research and Development (% Total Sales)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Novartis</td>
<td>$57,996</td>
<td>$7,331</td>
<td>13%</td>
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<td>2</td>
<td>Pfizer</td>
<td>$49,605</td>
<td>$8,393</td>
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<td>Roche</td>
<td>$50,216</td>
<td>$9,430</td>
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<td>Sanofi</td>
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<td>Merck</td>
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<td>Johnson and Johnson</td>
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<td>7</td>
<td>GlaxoSmithKline</td>
<td>$25,315</td>
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<td>AstraZeneca</td>
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<td>Gilead</td>
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<td>Takeda</td>
<td>$13,711</td>
<td>$2,768</td>
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Even smaller if only innovative product development is considered

“One of the great myths of the industry” that it costs $1B to develop a drug (CEO GlaxoSmithKline, 2014)
Explanations

• 1. High prices drive innovation
• 2. It’s the FDA’s fault
Meeting FDA’s ever-more-tolerant efficacy standard

• 1/3 new drugs approved on the basis of a single pivotal trial
• 2/3 approved based on studies lasting 6 mos or shorter
• 1/2 approved based on surrogate measures (vs actual clinical endpoints)
• Average number of patients studied to bring new drug to market
  – 1998-2001: >5,000
  – 2000-2010: 1,377
    • 1,708 (IQR: 968-3,195) for non-orphan-designated drugs
    • 438 (IQR: 132-915) for orphan-designated drugs

Downing et al., JAMA 2015; Tufts Center for the Study of Drug Development, 2002; Duijnhoven et al., PLoS Medicine, 2013
FDA speed

**Figure 3. Geographic Areas in Which Novel Therapeutics Approved in Multiple Markets Were First Approved for Use.**

- **U.S.**
  - 121 (64%)
  - 132 (86%)
  - 22 (14%)

- **Europe**
  - 110 (80%)
  - 27 (20%)

- **Canada**

**Review Times Of New Oncology Drugs Approved By The FDA And The EMA, 2003-10**

- Velcade
- Erbitux
- Alimta
- Avastin
- Vidiara
- Claraz
- Kepivance
- Tarceva
- Revlimid
- Aranora
- Nexavar
- Sutent
- Sprycel
- Vectibx
- Tykerb
- Tasigna
- Taritcon
- Treanda
- Firmagon
- Mozobil
- Affini
- Venzent
- Arzerra

**FDA speed**

Roberts et al., *Health Affairs*, 2011, Downing et al., *NEJM*, 2012
>2/3 of new drugs approved via expedited pathway in 2017

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<thead>
<tr>
<th>2017 NMEs</th>
<th>First-in-Class</th>
<th>Orphan</th>
<th>Fast Track</th>
<th>Priority Review</th>
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Explanations

1. “High prices drive innovation”
2. “It’s the FDA’s fault”
3. “High prices reflect value”
Fixed-dose combos covering 7 therapeutic areas

**Cardiovascular**
- Exforge = amlodipine + valsartan
- Diovan HCT = valsartan + HCTZ
- Bidil = isosorbide dinit + hydralazine
- Edarbyclor = Azilsartan + chlorthalidone
- Exforge HCT = amlodipine + valsartan + HCTZ
- Micardis HCT = telmisartan + HCTZ
- Lotrel = amlodipine
- Hyzaar = losartan + HCTZ
- Tarka = trandolapril + verapamil
- Caduet = amlodipine + atorvastatin
- Avalide = irbesartan + HCTZ
- Simcor = niacin + simvastatin
- Advicor = niacin + lovastatin
- Benicar HCT = olmesartan + HCTZ
- Azor = olmesartan + amlodipine
- Tribenzor = olmesartan + amlodipine + HCTZ

**Pain**
- Vimovo = naproxen + esomeprazole
- Duexis = ibuprofen + famotidine
- Arthrotec 75 = diclofenac + misoprostol
- Norco = hydrocodone + acetaminophen
- Vimovo = hydrocodone + acetaminophen
- Vicodin = hydrocodone + acetaminophen
- Vicodin ES = hydrocodone + acetaminophen
- Percocet = oxycodone + acetaminophen

**Endocrine**
- Actoplus MET = pioglitazone + metformin
- Fosamax Plus D = alendronate + VitD3

**Antibiotic**
- Pylera = bismuth + MNZ + tetracycline

**Urologic**
- Jalyn = dutasteride + tamsulosin

**Gastrointestinal**
- Zegerid = omeprazole + sodium bicarb

>600,000 Medicare beneficiaries in 2015
~$825 million in excess spending in 2015 in Medicare alone

Sacks, Lee, Kesselheim, Avorn, JAMA 2018
# ICER Value-Based Pricing in 2017

<table>
<thead>
<tr>
<th>Drug</th>
<th>Listed Price</th>
<th>ICER Value-based Price</th>
<th>Difference (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sacubitril/valsartan (Entresto)</td>
<td>$4,560/yr</td>
<td>$4,168</td>
<td>9%</td>
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<tr>
<td>PCSK9 Inhibitors</td>
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<tr>
<td>alirocumab: $14,600/yr</td>
<td></td>
<td>$2,177</td>
<td>85%</td>
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<td>evolocumab: $14,100/yr</td>
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<tr>
<td>Carfilzomib (Kyprolis)</td>
<td>$1,862/unit</td>
<td>$673</td>
<td>64%</td>
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<tr>
<td>Ixazomib (Ninlaro)</td>
<td>$2,190/unit</td>
<td>$181</td>
<td>94%</td>
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</table>
Explanations

1. “High prices drive innovation”
2. “It’s the FDA’s fault”
3. “High prices reflect value”

It’s because we allow pharmaceutical companies to charge whatever the market will bear, and at the same time permit strategies that undercut competition or hinder payors’ abilities to provide counterweights that might reduce high prices.
What can we do about it?

• A combination of different issues
• 4 major periods
  – Preapproval
  – Market exclusivity period
  – Transition to generic drugs
  – Multisource production period
Period 1: Brand-name market exclusivity

• All new drugs guaranteed ~6-7 years of market exclusivity – no competition
  – New antibiotics get 11-12 years
  – Biologics get 12 years
• Drugs protected by patents lasting 20 years
• Median market exclusivity for small-molecule (non-biologic) drugs is 12.5 years
  – 14.5 years for first-in-class products

Wang, Liu, Kesselheim, JAMA IM, 2015
Limits on public payors...

• FDA does not regulate drug prices or any economics of the industry
• Medicare (45M, 29% of nation’s drug expenditure) cannot use a national formulary or negotiate drug prices
  – 6 protected drug classes
• Medicaid (75M) cannot exclude most FDA approved drugs from coverage
  – Gets automatic rebate; individual states can negotiate supplemental rebates
• VA can use formulary exclusions to negotiate directly with manufacturers
  – Initial prices 40% below those paid by Medicare Part D plans
  – VA price excluded from Medicaid rebate calculation
... and private insurers, too

- ~200 million people
- Annual deductibles, co-payments, co-insurance ("out-of-pocket" costs)
- Formularies, administered by pharmacy benefit managers
- BUT ... lack of comparative effectiveness information at the time of approval
  - Sample of 197 drugs approved 2000-2010: 51% had CE info at time of approval, including 33% of drugs for which other treatment options existed
    - State laws requiring coverage of certain protected drugs
      - NCSL 2009: 36/50 states require coverage of off-label use of cancer drugs
Coupons and Patient Assistance

Availability of Lower-Cost Alternatives to Brand-Name Drugs for Which Coupons Are Offered.

Data are for the 374 drug coupons advertised at www.internetdrugcoupons.com in March 2013. FDA denotes Food and Drug Administration.

Ross and Kesselheim, NEJM, 2013
PBM}s … good or bad?

- Negotiate rebates from mfrs, discounts from retailers
- Encourage use of generics and cheaper brands
- Patience adherence, reduce waste
- Aggressive price negotiation is not the norm (fees can be based on given payer’s spending on drugs)
- Lead to increases in “list prices”
Solutions: Medicare negotiation

• Competitive licensing (HR 1046)
  – Medicare Part D price negotiation, taking into account:
    • Comparative clinical and cost-effectiveness
    • Budgetary impact of providing coverage
    • Unmet need
    • Global sales revenue
  – If unable to successfully negotiate...“Secretary shall authorize the use of any patent, clinical trial data, or other exclusivity granted by the Federal government with respect to such drug as the Secretary determines appropriate for purposes of manufacturing such drug for sale under a prescription drug plan or MA–PD plan. Any entity making use of a competitive license to use patent, clinical trial data, or other exclusivity under this section shall provide to the manufacturer holding such exclusivity reasonable compensation

• Mandatory arbitration
Other Proposals

• International Pricing Index (ANPRM, fall 2018)
  – Part B drug prices comparable to other economically similar countries (2020-2025)
  – Allow private-sector vendors to negotiate prices for drugs

• Eliminating the requirement that Medicare cover all FDA-approved products in 6 drug classes (Blueprint)

• Eliminate Medicaid rebate cap (Blueprint)
  – ~$100 million in foregone savings in 2017

• Eliminate certain drug rebates by revoking anti-kickback statute safe harbor for rebates paid by drug mfrs to PBMs, PDPs, and Medicaid MCPs (Jan 2019)

See Sarpatwari and Kesselheim JAMA 2019; Sarpatwari Avorn Kesselheim JAMA 2018
Other ideas

• Inflation-based rebates in Part B  
  – CBO estimate $1.5B savings from 2019-2028

• Shift dual-eligible patients back from Medicare to Medicaid  
  – CBO estimate $150B savings from 2019-2028

• Shift Part B drugs to Part D
Part B to Part D shift

Rx prices were >46% lower in other high-income countries

International Price Comparison for Part B Drugs

- Foreign prices were available for 69 drugs (out of 75 total in study cohort)
- Drug prices in high-income countries were 46-60% lower than those in Part B
- US to foreign price ratio was 1.7-2.2x (consistent with ASPE’s est. of 1.8x based on sample of 25 drugs)

“Outcomes-Based Contracts”?

Advantages

• Opportunity to pay for drugs only in patients in which “appear to work”

Limitations

• Outcomes measurement limitations (short-term, observable in claims data, surrogates)
• Can account for in price-setting
• Costly to implement
• Unclear application to patient out-of-pocket costs

Seeley and Kesselheim, Commonwealth Fund Issue Brief, 2017
More extreme solutions

• Use current pathways for US government to intervene for essential patent-protected medicines
  – Ex.: Section 1498 “government patent use” for a reasonable royalty (ex: ciprofloxacin/anthrax)
  – “March-in rights”

State interventions

• Medicaid formulary 1115 waiver – tried by Massachusetts, blocked by CMS
• Drug price gouging law in MD – blocked by federal court
• California AB-265 – prevent drug coupon use when generic available
• Transparency laws (VT, NV, CA, OR, CT, ME)
• NY: DOH authorized to identify and refer high-cost drugs to a drug utilization review board for a determination of a target rebate amount (2017)
  – Implemented in Massachusetts in 2019
• Louisiana hep C drug purchase

See Sommers and Kesselheim, NEJM 2018; Hwang, Kesselheim, Sarpatwari, JAMA 2017; Greene, NEJM 2017
Physician/patient-level interventions

• Re-evaluate widespread use of drug coupons, DTCA, free samples
  – Mandate disclosure of prices in DTCA (Blueprint)
• Integrating value-based prescribing into physicians’ professional education or through electronic medical record point-of-care reminders
• Accountable Care Organizations can provide an opportunity to pair health services costs and drug costs so that physicians benefit from prescribing drugs optimally rather than from prescribing drugs that do not add value
• Produce and actively disseminate better information about the clinical and economic value of drugs

Kesselheim et al., JAMA, 2016
Academic detailing

• **Goal:** To close the gap between:
  • the best available evidence
  • actual clinical practice

• ...so that clinical decisions are based only on the most current and accurate evidence on:
  • Efficacy
  • Safety
  • Cost-effectiveness

• **Often supported by** a public health agency or a non-profit health care system like Kaiser that is interested in improving clinical outcomes
Period 2: Brand-to-generic transition

- Generic drugs are the only type of competition that consistently and substantially lowers prescription drug prices
  - Emerge after market exclusivity period ends (lawsuits initiated by generic drug manufacturer)
  - Abbreviated FDA approval process, state Drug Product Selection laws facilitate automatic substitution

- Barriers to generic drug entry
  - Patent term restoration, pediatric exclusivity extension
  - Pay-for-delay settlements of lawsuits
  - “Life cycle management”
    - Secondary patenting
    - Product hopping

Kesselheim et al, JAMA IM, 2017; Vokinger et al, JAMA IM, 2017
Secondary patenting

• Lopinavir/Ritonavir
  – 2 patents covering active ingredients
  – 49 patents covering different compositions/formulations
  – 22 patents covering different intermediate compounds
  – 4 patents covering different polymorphs
  – 6 patents covering different prodrugs
  – 31 patents covering different methods of treatment of HIV and other diseases

• Potential to extend market exclusivity by 12 years or more
Product hopping

• 2003: FDA approves memantine (Forest)
• 2010: FDA approves memantine XR (Forest)
• 2013: Forest launches memantine XR
• Feb 2014: Forest announces anticipated August discontinuation of memantine
• July 2015: Expiration of memantine patent term, anticipated generic launch
• 2029: Expiration of memantine XR patents
“Tertiary” patents

- Drug delivery devices
  - Inhalers, injector pens, patches
- 2000: 42 drug-device combo products, 85 associated patents (34% tertiary)
- 2016: 127 drug-device combo products, 844 patents (57% tertiary)

<table>
<thead>
<tr>
<th>Year</th>
<th>All patents</th>
<th>Tertiary patents, N (%)</th>
<th>All drug products listing one or more patents</th>
<th>Drug products listing a drug delivery device patent, N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000</td>
<td>916</td>
<td>27 (3)</td>
<td>614</td>
<td>18 (3)</td>
</tr>
<tr>
<td>2005</td>
<td>1,593</td>
<td>61 (4)</td>
<td>835</td>
<td>35 (4)</td>
</tr>
<tr>
<td>2010</td>
<td>2,069</td>
<td>135 (7)</td>
<td>997</td>
<td>59 (6)</td>
</tr>
<tr>
<td>2016</td>
<td>3,464</td>
<td>295 (9)</td>
<td>1,135</td>
<td>109 (10)</td>
</tr>
</tbody>
</table>

*Products were counted by new drug application (NDA) numbers.*

Beall & Kesselheim, *Nature Biotechnology*, 2018
Market exclusivity term

- Patent app filed
- IND approved
- NDA approved
- Patent issues
- NDA filed
- HWA Excl
- Orphan Drug Act
- Market Exclusivity Period
- PTR
- Generic entry?
- "Later-issued" (Orange Book-listed) patents

YEAR

0 3 6 9 12 15 18 21 24 27
Market exclusivity term

- Patent app filed
- IND approved
- NDA approved
- Patent issues
- NDA filed

Market Exclusivity Period

- "Later-issued" (Orange Book-listed) patents
- Para IV challenge

HWA Excl

Orphan Drug Act

PTR

Generic entry!

YEAR

-1 0 3 6 9 12 15 18 21 24 27
Other strategies

• Restrictions on drug distribution
  – 150 inquiries to FDA from generic manufacturers unable to obtain samples

• Citizens petitions
  – 2011-2015: 124 CPs relating to generic applications, 87% from brand-name manufacturers (92% ultimately denied)
    • Vancocin tablets: 24 CPs from 2006-2012
Solutions

• CREATEES Act
• An eligible product developer may bring a civil action against the license holder for a covered product seeking relief under this subsection in an appropriate district court of the United States alleging that the license holder has declined to provide sufficient quantities of the covered product to the eligible product developer on commercially reasonable, market-based terms
  – If subject to REMS/ETASU then needs formal covered product authority from Secretary of HHS
  – Defense if not manufacturing or no inventory
  – Court will award fines
Solutions

• CREATEES Act

• Patent Trial and Appeals Board to re-examine granted patents before litigation
Patent Trial and Appeals Board

• 2011 America Invents Act
  – There is “a growing sense that questionable patents are too easily obtained and are too difficult to challenge.”

• Administrative body allowing any party to challenge validity of patented claims
  – Patent relating to the anesthetic agent propofol (Diprivan), but one that covers the rubber stopper used in the drug’s holding container, not the drug itself

• Advantages:
  1. Starts with PTAB, not examiner
  2. PTAB must decide within 12 months
  3. Allows for limited “discovery” (esp. depositions)
  4. Both parties can appeal to Fed. Cir.
  5. Less costly ($500K vs $5.5M)

Disappointing Application to Drug Patents

Table 1 Disposition of inter partes review proceedings challenging Orange Book-listed patents

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Number, n (%)</th>
<th>Total N = 362</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not instituted (merits)</td>
<td>68 (19%)</td>
<td></td>
</tr>
<tr>
<td>Not instituted (procedural)</td>
<td>32 (9%)</td>
<td></td>
</tr>
<tr>
<td>Settlement</td>
<td>50 (14%)</td>
<td></td>
</tr>
<tr>
<td>Final written decision</td>
<td>89 (25%)</td>
<td></td>
</tr>
<tr>
<td>Pending</td>
<td>117 (32%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>6 (2%)</td>
<td></td>
</tr>
</tbody>
</table>

- 274 (76%) filed by generic drug manufacturers
- Among 89 FWDs, 38 (43%) had all petitioned claims invalidated, 44 (49%) had none invalidated, and 7 (8%) had some invalidated
  - Related to 25 OB-listed patents: 2 active ingredient, 7 formulation, and 16 other (incl methods of use)
- 38 decisions with all invalidated associated with 18 drugs, 9 of which had other non-instituted petitions and 7 had other OB-listed patents

Darrow, Beall, Kesselheim, *Applied Health Economics and Health Policy*, 2018
Solutions

• CREATE Act

• Patent Trial and Appeals Board to re-examine granted patents before litigation

• Change rules related to CPs

• Block pay-for-delay deals
Protecting Consumer Access to Generics (HR 1499)

• Unlawful for an NDA or BLA holder and a subsequent filer to enter into, or carry out, an agreement resolving or settling a covered patent infringement claim on a final or interim basis if under such agreement— (1) a subsequent filer directly or indirectly receives from such holder anything of value, including an exclusive license; and (2) the subsequent filer agrees to limit or forego research on, or development, manufacturing, marketing, or sales, for any period of time
  – Except if the value is compensation for other goods/services that the subsequent filer has promised to provide
More ideas

• Orange Book reform
  – No devices
  – Removal of patent relating to older formulations

• Purple Book reform
  – List patent information

• 180-day exclusivity changes (FAIR Act, BLOCKING Act)

See Sommers and Kesselheim, NEJM 2018; Hwang, Kesselheim, Sarpatwari, JAMA 2017; Greene, NEJM 2017
Period 3: Generic Competition

<table>
<thead>
<tr>
<th>Year</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>≥10</th>
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<tbody>
<tr>
<td>2008</td>
<td>81</td>
<td>73</td>
<td>57</td>
<td>54</td>
<td>50</td>
<td>39</td>
<td>47</td>
<td>29</td>
<td>34</td>
<td>29</td>
</tr>
<tr>
<td>2009</td>
<td>78</td>
<td>77</td>
<td>50</td>
<td>52</td>
<td>49</td>
<td>41</td>
<td>39</td>
<td>36</td>
<td>23</td>
<td>27</td>
</tr>
<tr>
<td>2010</td>
<td>86</td>
<td>77</td>
<td>52</td>
<td>47</td>
<td>47</td>
<td>43</td>
<td>30</td>
<td>27</td>
<td>37</td>
<td>21</td>
</tr>
<tr>
<td>2011</td>
<td>89</td>
<td>69</td>
<td>58</td>
<td>50</td>
<td>46</td>
<td>37</td>
<td>40</td>
<td>23</td>
<td>23</td>
<td>21</td>
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<tr>
<td>2012</td>
<td>77</td>
<td>78</td>
<td>56</td>
<td>47</td>
<td>40</td>
<td>41</td>
<td>38</td>
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<tr>
<td>2013</td>
<td>109</td>
<td>86</td>
<td>78</td>
<td>62</td>
<td>42</td>
<td>26</td>
<td>29</td>
<td>25</td>
<td>18</td>
<td>17</td>
</tr>
<tr>
<td>2014</td>
<td>88</td>
<td>77</td>
<td>68</td>
<td>54</td>
<td>51</td>
<td>37</td>
<td>31</td>
<td>19</td>
<td>15</td>
<td>14</td>
</tr>
</tbody>
</table>

Average: 87 77 60 52 46 38 36 26 25 21
Small markets: 87 77 63 56 47 38 39 27 23 28
Large markets: 84 74 54 47 46 40 35 25 24 19

Dave, Hartzema, Kesselheim, *NEJM*, 2017
Lack of vibrant generic drug market

Gupta, Kesselheim, et al., JAMA IM, 2016
Solutions

• Import generics from well-regulated markets
  – When price spikes are equivalent to ‘shortages’

Fralick, Avorn, Kesselheim, *NEJM* 2017
Importation?

• FDA already exercises enforcement discretion to respond to shortages
• 2003 Medicare Modernization Act authorized import from Canada if HHS Secretary certified drugs as safe
• 2012 FDA Safety and Innovation Act gave the FDA authority to enter into agreements to recognize drug inspections conducted by foreign regulatory authorities if the FDA determined those authorities are capable of conducting inspections that met US requirements
Affordable and Safe Prescription Drug Importation Act

• Canadian pharmacies and wholesale distributors can become “certified foreign” sellers by paying a user fee and:
  – Being in Canada
  – Being a distributor of prescription drugs offered for importation
  – Being established for 5 years or more
  – Providing medications only if there is a valid prescription
  – Being in compliance with applicable Canadian laws and regulations
  – Conducting regular quality assurance
  – Allowing regular laboratory testing
  – Notifying all parties of product recalls
  – Having a process for resolving rule violations
  – Not selling products that are illegal in Canada
  – Meeting additional criteria implemented by the Health and Human Services secretary

• GAO study of outcomes after 18 mos, expand to include other OECD countries after 2 years
## Practical?

<table>
<thead>
<tr>
<th>Category</th>
<th>Number of drugs</th>
<th>0 generic competitors</th>
<th>1 generic competitor</th>
<th>2 generic competitors</th>
<th>3 generic competitors</th>
</tr>
</thead>
<tbody>
<tr>
<td>U.S. drugs with insufficient generic competition</td>
<td>69*</td>
<td>35</td>
<td>13</td>
<td>7</td>
<td>14</td>
</tr>
<tr>
<td>U.S. generic drugs with insufficient competition made by at least one different manufacturer approved outside the U.S.**</td>
<td>44</td>
<td>18</td>
<td>10</td>
<td>5</td>
<td>11</td>
</tr>
<tr>
<td>EMA or Health Canada</td>
<td>22</td>
<td>7</td>
<td>5</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>Other regulators</td>
<td>37</td>
<td>17</td>
<td>7</td>
<td>3</td>
<td>10</td>
</tr>
<tr>
<td>Could reach sufficient competition (defined as 4 or more different manufacturers) with foreign regulator-approved sources of that drug**</td>
<td>23</td>
<td>6</td>
<td>2</td>
<td>4</td>
<td>11</td>
</tr>
<tr>
<td>EMA or Health Canada</td>
<td>11</td>
<td>3</td>
<td>0</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Other regulators</td>
<td>15</td>
<td>3</td>
<td>0</td>
<td>2</td>
<td>10</td>
</tr>
</tbody>
</table>
Solutions

• Import generics from well-regulated markets
  – When price spikes are equivalent to ‘shortages’

• Apply regulatory attention
  – Fund generic drug science and FDA Office of Generic Drugs
  – Expedite review of generic applications when three or fewer drugs in the market

• Follow-on biologics
Common perceptions

• Better pricing mechanisms will undercut innovation
  – Innovation is often performed in academic institutions and supported by public investment such as the National Institutes of Health
  – Loss of market exclusivity protection was the “most important predictor” of the arrival of a new product and the number of new product introductions
  – Brand-name pharmaceutical manufacturers ~22% profits in 2015; rest of Fortune 500 ~7%

• Better pricing is politically impossible
  – 72% of Americans feel that drug costs are unreasonable and 74% feel drug companies put profits before people (Aug 2015 KFF poll)

Summary points

• Prescription drugs can be transformative and take substantial time and resources to develop, but increasing costs for patients and system

• Drugs prices set by manufacturer at high levels due to lack of effective “competition” in market due to market exclusivities, restrictions on payors

• Just because a drug is generic does not mean it’s inexpensive