Division of
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Department of Medicine, Brigham & Women's Hospital, Harvard Medical School

Strategies for Ensuring Patient Access to Affordable Drug Therapies

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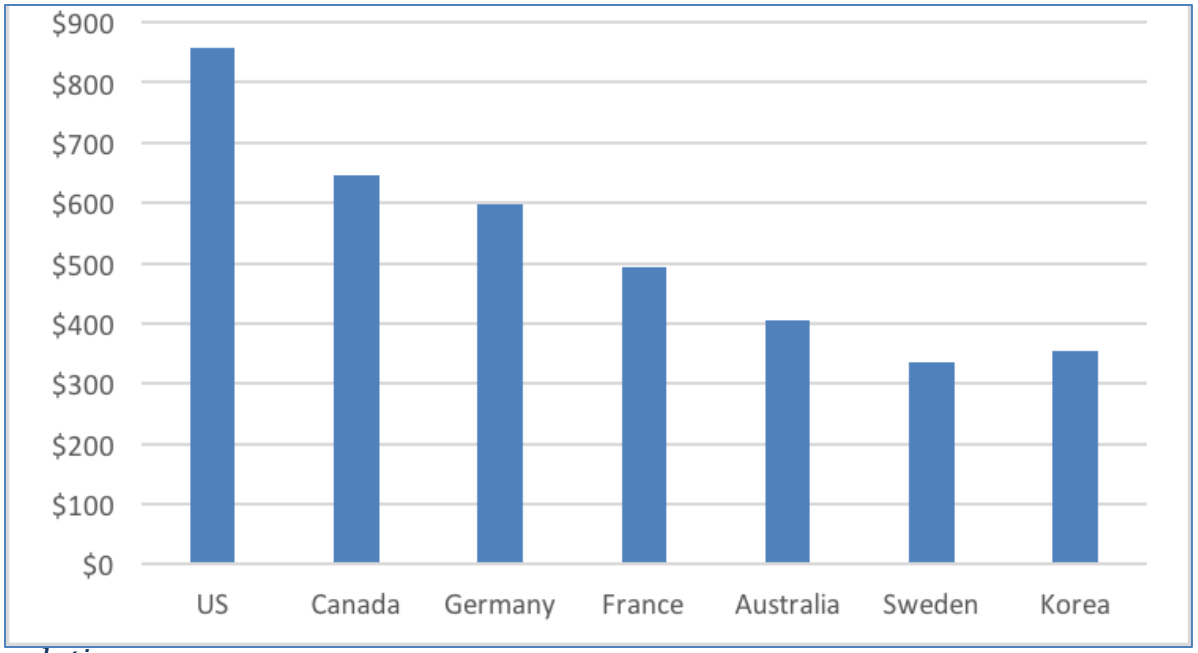
What is PORTAL?

- 2 full-time faculty; 10 affiliated faculty in medicine, business, law, and economics; 5 post-docs; numerous students
- Focus on research at intersection of law, therapeutics, and public health
- No one in our Division has personal financial relationships with any pharmaceutical company
- Current research funding from Greenwall Faculty Scholars Foundation in Bioethics, FDA Office of Generic Drugs, Harvard Program in Therapeutic Science, Laura and John Arnold Foundation, Commonwealth Fund
  - Past research funding from FDA CDRH, Harvard Clinical and Translational Science Center, AHRQ, Robert Wood Johnson Foundation, CVS Caremark

Prescription Drug Spending in the US

- Rose 13% in 2014 to $374 billion
- Constitutes 19% of employer-based insurance benefits
- International per capita comparisons
  - US: **$858**; avg 19 industrialized countries: **$400**



-OECD (2015)

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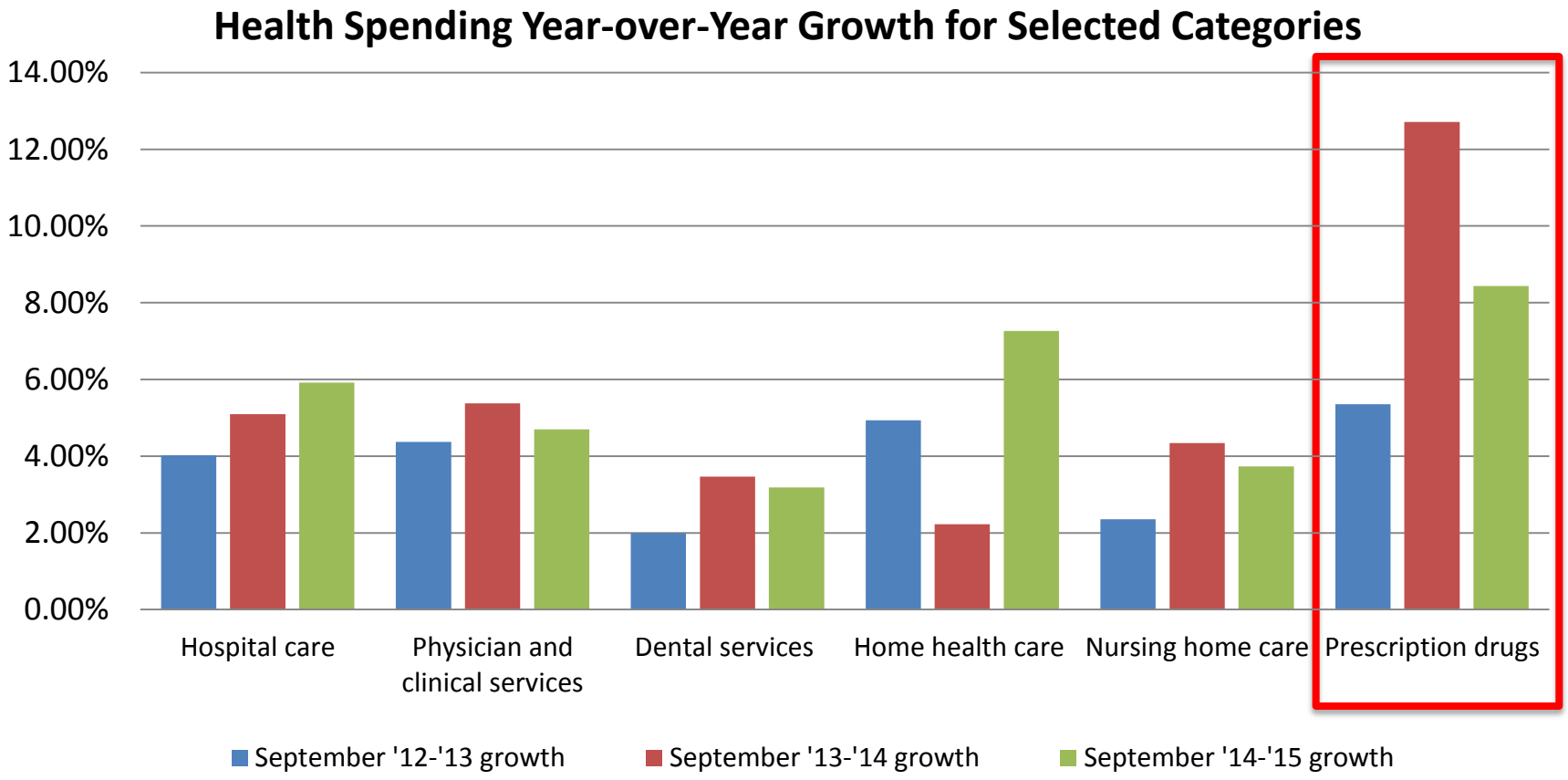
Drug Spending vs. Other Health Care Sectors



Source: Altarum monthly national health spending estimates

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Brand-Name Drugs

- 12% prescriptions, 72% of spending
- 127% increase in price from 2008-2014 of most commonly used brand-name drugs
  - 11% increase in CPI, 26% increase in aggregate health care spending

Not limited to brand-name drugs

- Changes in price of >21,000 generic products (2008-2015)
  - 400 (2%) increased more than 1,000%
  - 11,393 (54%) remained constant

-Connecture

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 2015 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

Shrank et al, Archives Int Med 2006; Gagne et al, Annals of Int Med, 2014; DiJulio et al., Kaiser Family Foundation

ORIGINAL RESEARCH | Annals of Internal Medicine

Comparative Effectiveness of Generic and Brand-Name Statins on Patient Outcomes

A Cohort Study

Joshua J. Gagne, PharmD, ScD; Niteesh K. Choudhry, MD, PhD; Aaron S. Kesselheim, MD, JD, MPH; Jennifer M. Polinski, ScD, MPH; David Hutchins, MBA, MHSA; Olga S. Matlin, PhD; Troyen A. Brennan, MD; Jerry Avorn, MD; and William H. Shrank, MD, MSHS

Table 2. **Hazard Ratios for Outcomes Among Generic Versus Brand-Name Statin Recipients**

Outcome	Hazard Ratio (95% CI)	
	Unmatched (Crude)	Propensity Score–Matched
Composite end point	0.94 (0.88–1.00)	0.92 (0.86–0.99)
Hospitalization for an acute coronary syndrome	0.92 (0.86–0.98)	0.92 (0.85–0.99)
Hospitalization for stroke	1.04 (0.85–1.26)	0.96 (0.78–1.18)
Death from any cause	1.14 (0.85–1.54)	0.95 (0.69–1.30)

Why?

- 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

Period 1: Brand-name market exclusivity

- All new drugs guaranteed about 6-7 years of market exclusivity
  - New antibiotics get 11-12 years
  - Biologics get 12 years
- Drugs protected by patents lasting 20 years
- The median length of post-approval market exclusivity for small-molecule drugs is 12.5 years (IQR: 8.5-14.8 years) for widely-used drugs and 14.5 years (IQR: 13.3-15.8 years) for highly innovative, first-in-class drugs

Wang, Liu, Kesselheim, JAMA IM, 2015

Limits on gov't payors' ability to negotiate

- FDA has no authority to regulate drug prices or any economics of the industry
- Medicare (40M, 29% of nation's drug expenditure) cannot negotiate drug prices
  - 2003 Medicare Modernization Act: (1) HHS Secretary cannot "interfere with the negotiations," "institute a price structure" for Part D drugs; (2) limits on formulary adjustments
- Medicaid (60M) pays acquisition costs, gets rebate; individual states can negotiate supplemental rebates (no formulary exclusions)
- VA negotiates directly with manufacturers
  - Prices 40% below those paid by Medicare Part D plans
  - VA price excluded from Medicaid rebate calculation

Other payors, too

- 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

Solutions?

- Give greater latitude in making clinically appropriate formulary choices
  - "Therapeutic substitution"
- Authorize Medicare to negotiate the prices for drugs
- Produce better information about the clinical and economic value of drugs
  - Government-funded technology assessment activities provide support for needed comparative studies and evaluate new products in light of their comparative cost-effectiveness analysis
  - Info used by government and private payors to help determine their responsiveness to company-set prices, make determinations about formulary rules and exclusions, and educate physicians and patients

Physician/patient interventions

- Re-evaluate widespread use of drug coupons, DTCA, free samples, “DAW” prescriptions
- 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

Safety net

- Pathways for US government to intervene when prices set unreasonably high for essential patent-protected medicines
  - Bayh-Dole Act
  - Section 1498 “government patent use” (ex: ciprofloxacin/anthrax)

Kapczynski and Kesselheim, Health Affairs, 2016; Treasure, Avorn, Kesselheim, JAMA 2016

Period 2: Brand-to-generic transition

- The only type of competition that consistently and substantially lowers prescription drug prices occurs from the availability of generic drugs, which emerge after the exclusivity period ends
  - Abbreviated FDA approval process
  - Action of state Drug Product Substitution laws through which many states allow automatic interchange of A-rated generic products

Market exclusivity extensions

- Patent term restoration
  - One half of the time from the initiation of clinical trials to the filing of the NDA, plus the full time the FDA took to review the NDA (caps at 5 yrs per extension, 14 yrs total)
- Pediatric exclusivity extension
  - 6 mos for fulfilling Pediatric Written Request
- Product hopping

"Life-cycle management"

- Secondary patenting

Patents And Applications Covering Ritonavir And Lopinavir/Ritonavir

Patent categories	Ritonavir	Lopinavir	Lopinavir/ritonavir	Ritonavir and/or lopinavir with other compounds	Total
Total	—[a]	—[a]	—[a]	—[a]	210
Base compound or active ingredient	1	1	0	0	2
RELATED CHEMICAL STRUCTURES AND COMPOSITIONS OR FORMULATIONS (81)					
Composition and formulation[b]	18	9	15	7	49
Intermediate compounds	13	9	0	0	22
Polymorphs	2	2	0	0	4
Prodrugs	2	2	1	1	6
MANUFACTURING METHODS AND PROCESSES (68)					
Processes[c]	36	27	5	0	68
METHODS OF TREATMENT OF HIV INFECTION AND OTHER DISEASES (31)					
First method of treatment or administration for HIV	4	4	5	5	18
New uses for HIV or other diseases	6	1	1	5	13
GENERAL PATENTS (28)					
General formulations	—[d]	—[d]	—[d]	—[d]	5
Processes and methods for preparing general formulations	—[d]	—[d]	—[d]	—[d]	11
Other technologies or test systems	—[d]	—[d]	—[d]	—[d]	12

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Amin and Kesselheim, Health Affairs, 2013

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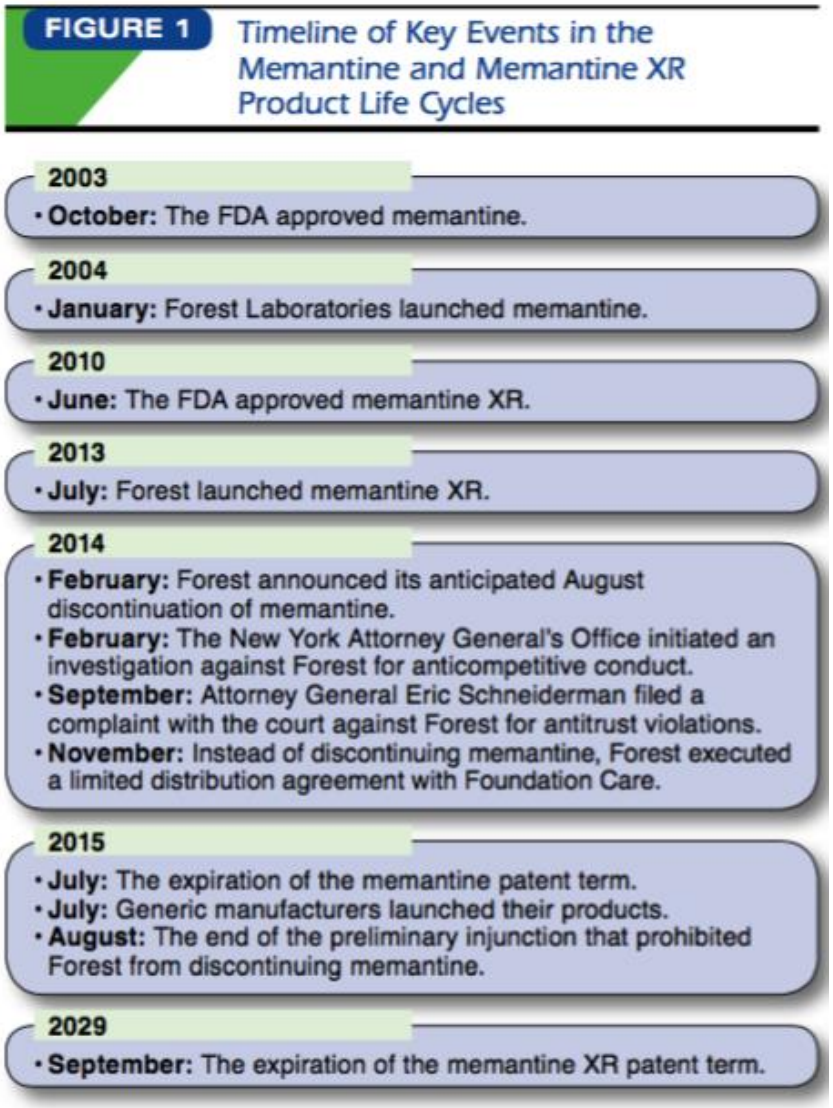
“Life-cycle management”

- Product hopping



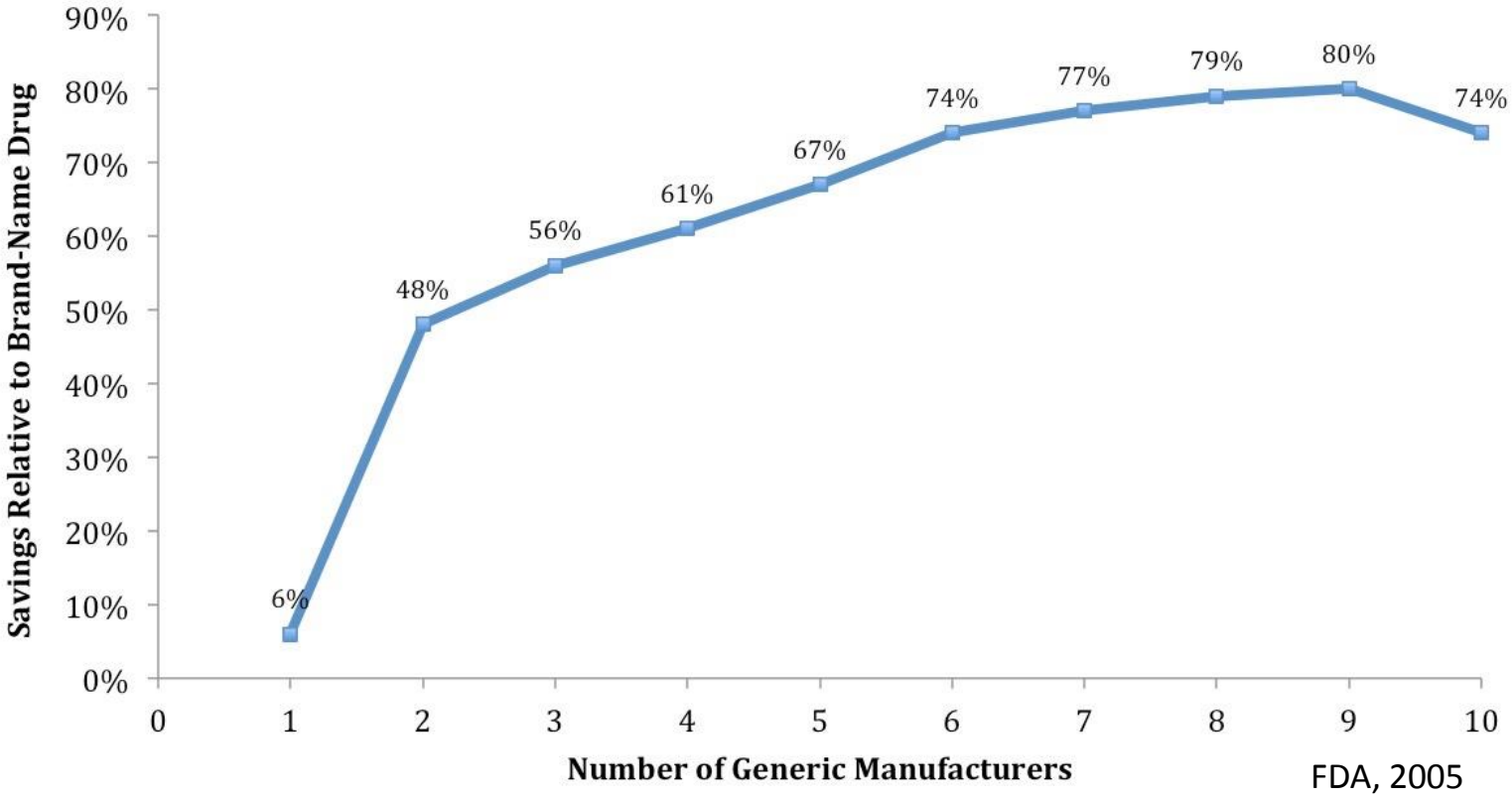
Capati and Kesselheim, JMCP, 2015

Some solutions

- Re-examine patents at time of Orange Book listing by Patent Trial and Appeals Board

- Better attention to entry of follow-on biologics

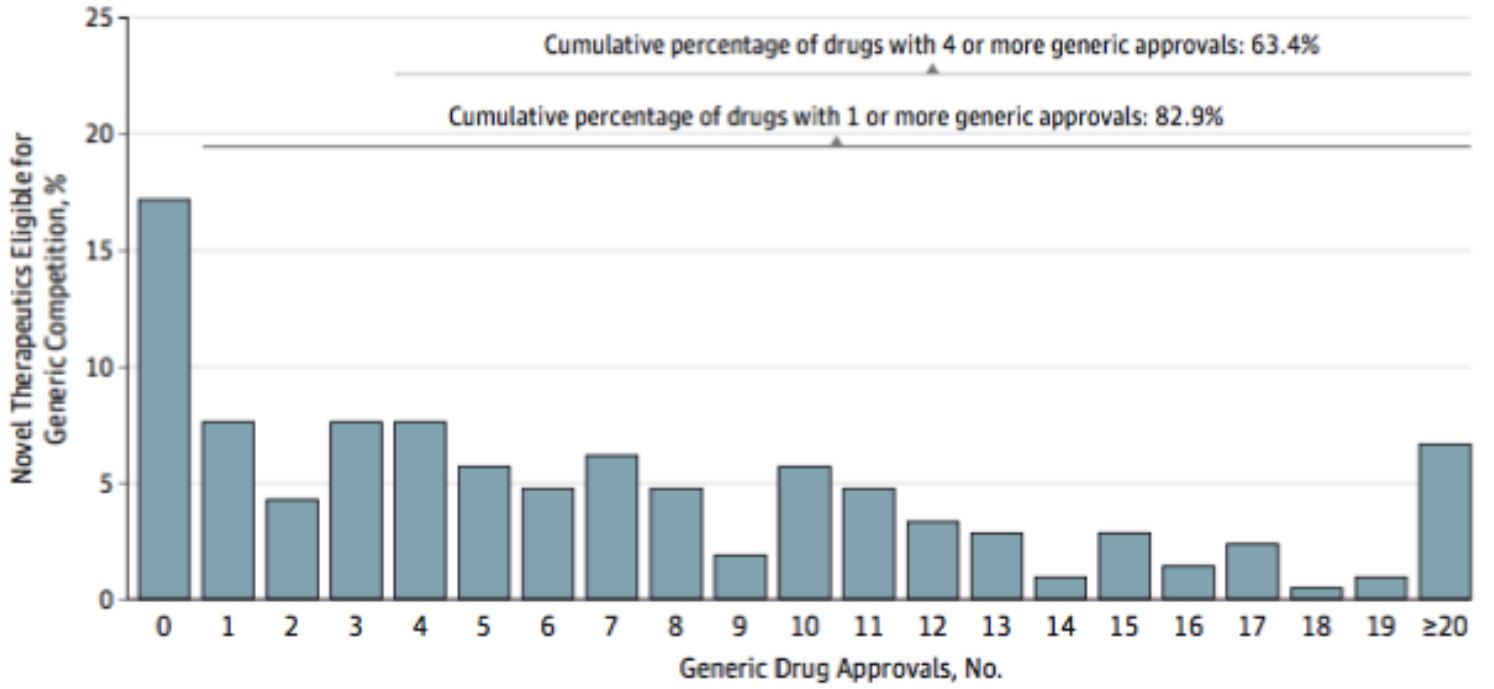
Period 3: Patent-free



FDA, 2005

Lack of vibrant generic drug market

Figure. Generic Drug Approvals for Novel Therapeutics Approved by the US Food and Drug Administration Eligible for Generic Competition.



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

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Solutions

- Importation from well-regulated markets
  - Price spikes equivalent to ‘shortages’
- Government purchasing contracts
- Regulatory attention
  - Funding of generic drug science
  - Expedited review of applications when four or fewer drugs in the market
- Re-examine branded ‘updates’
  - Unapproved drugs initiative
  - Drug/device combinations

Summary points

- Cost of drugs in US set by manufacturers based on what market will bear
- 3 different time periods: different issues, different solutions

Thank you!

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