

Economic Issues Underlying Recent but Persistent Drug Shortages in the US

Presentation to NASEM/FDA Workshop “Medical Product Shortages during Disasters: Opportunities to Predict, Prevent and Respond” – September 5, 2018

by

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Outline of Today's Discussion

- Defining and Identifying Drug Shortages – FDA and ASHP/Utah
- Quantifying and Interpreting “Classic” Drug Shortages
- “Disaster Shortages” -- Shortages Emanating from Natural Disasters – the September 2017 Hurricane Maria Decimating Puerto Rico
- Preliminary Thoughts on Issues and Challenges in Preventing and Managing “Classic” or “Disaster” Drug Shortages

What is a Shortage?

An Economic Perspective

- “Ran out of a drug, can’t get adequate replacement supply unless I deal with unlicensed suppliers”?
- Economic perspective: A shortage exists when, at any given market price, the quantity demanded by purchasers exceeds the quantity supplied by manufacturers.
- Conventional Econ 101 textbook competitive market dynamics: In response to a shortage, profit-maximizing firms raise prices, the quantity demanded falls, new suppliers enter or existing suppliers increase quantity because of expected profitability, and over time the combination of increased quantity supplied and reduced quantity demanded as prices increase eliminates the shortage.
- “Shortages” should be transitory in a “competitive” market. But the drug shortages appear to be quite persistent, not transitory
- “Competition” suggests: Need higher prices and both short-run supply and short-run demand responses to higher prices – but for many drugs, short-run supply and demand responses are limited. Long run responses?

Drugs in Short Supply: Historical Background

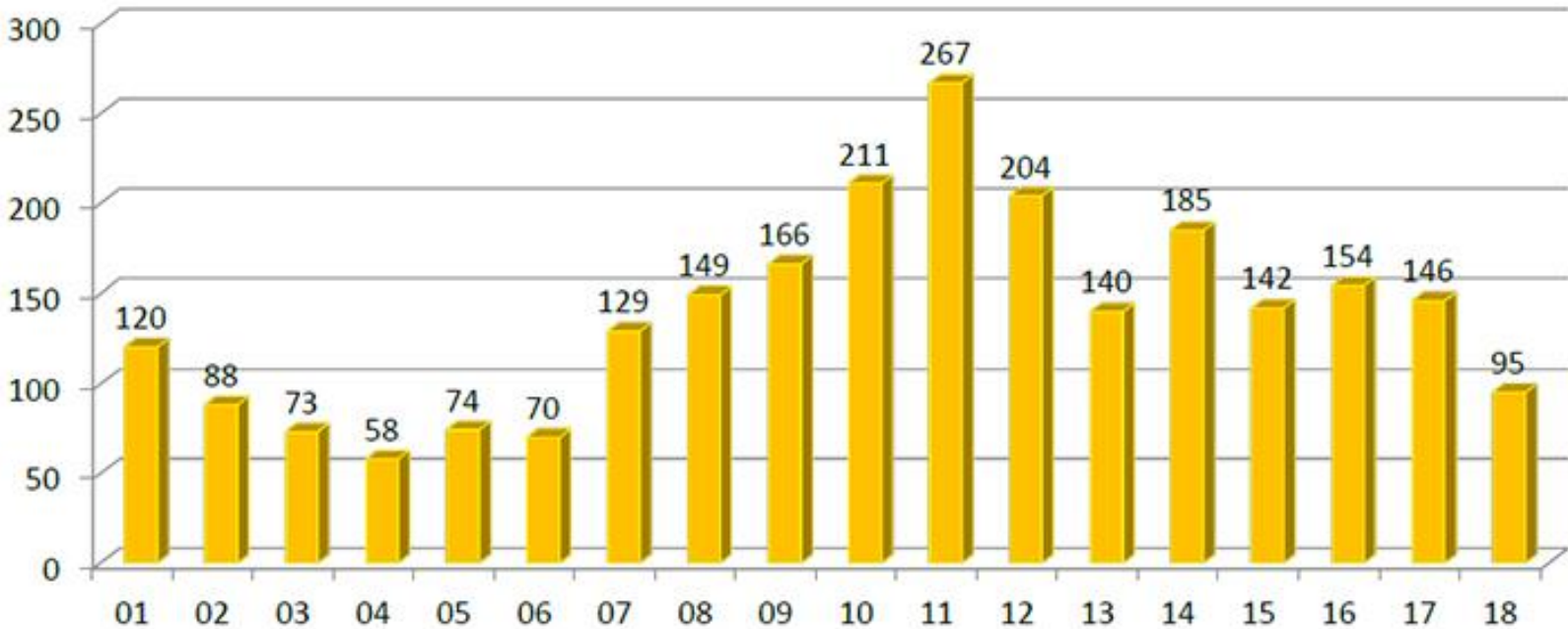
- The Drug Shortage Program at the US Food and Drug Administration (FDA) and the American Society of Health-System Pharmacists (ASHP) in collaboration with the University of Utah maintain websites that identify and provide detailed current and historical information on drugs in short supply.
- Previous presenters today have discussed differences in the FDA and ASHP/Utah metrics underlying reported drug shortages
- Let's look at numbers for “classic” drug shortages

FDA/Utah Information Service Reported Shortages

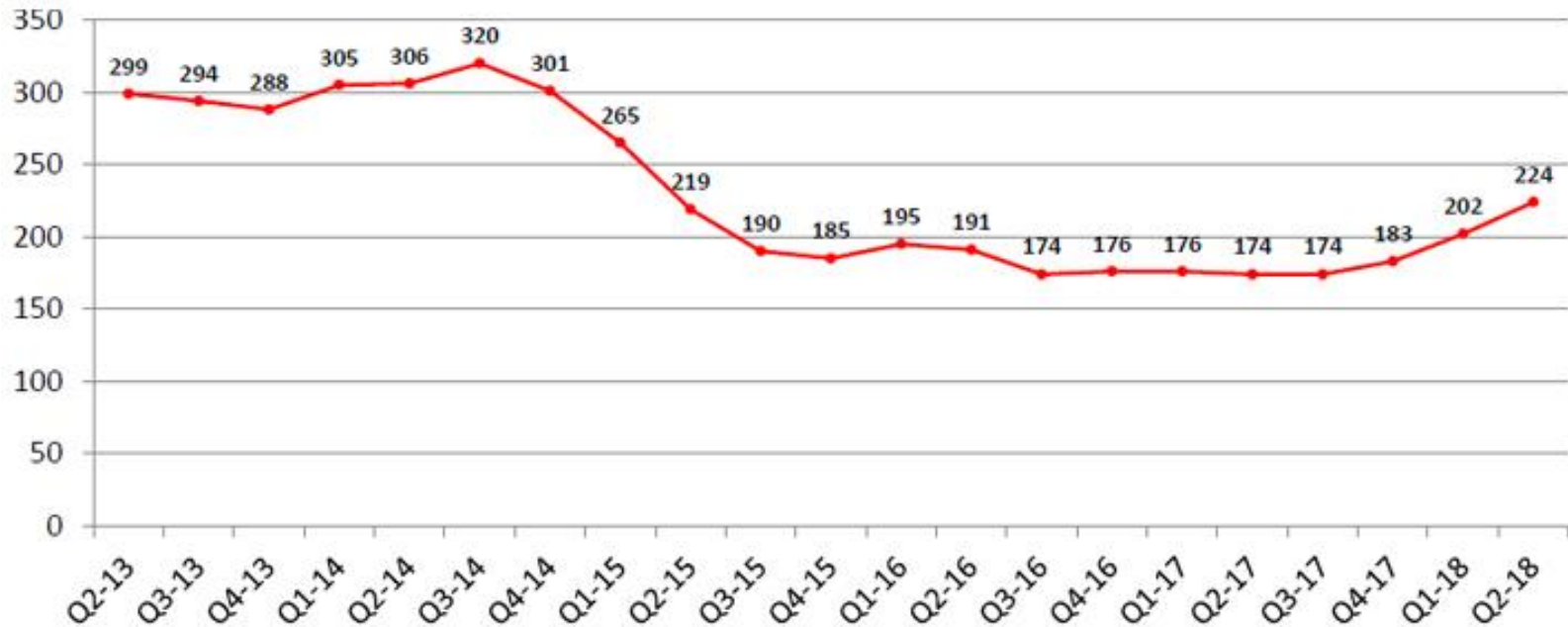
<u>Year</u>	<u>ASPH/Utah # Shortages</u>	<u>FDA No. Shortages</u>	<u>FDA No. Sterile Injectables</u>	<u>FDA %</u>
2005	74	60	30	50.0
2006	70	55	25	45.5
2007	129	92	42	45.7
2008	149	110	40	36.4
2009	166	157	75	47.8
2010	211	178	132	74.2
2013	140	126	98	77.8
2014	185	69	55	79.7

Source: ASPE Issue Brief , October 2011, Appendix A Table 1, p. 16. 2013 updates from American Society of Health-System Pharmacists, 4/21/13; FDA Current Drugs Shortages List, 4/21/13; 2014 <http://www.accessdata.fda.gov/scripts/drug> shortages

National Drug Shortages: Annual New Shortages by Year January 2001 to June 30, 2018

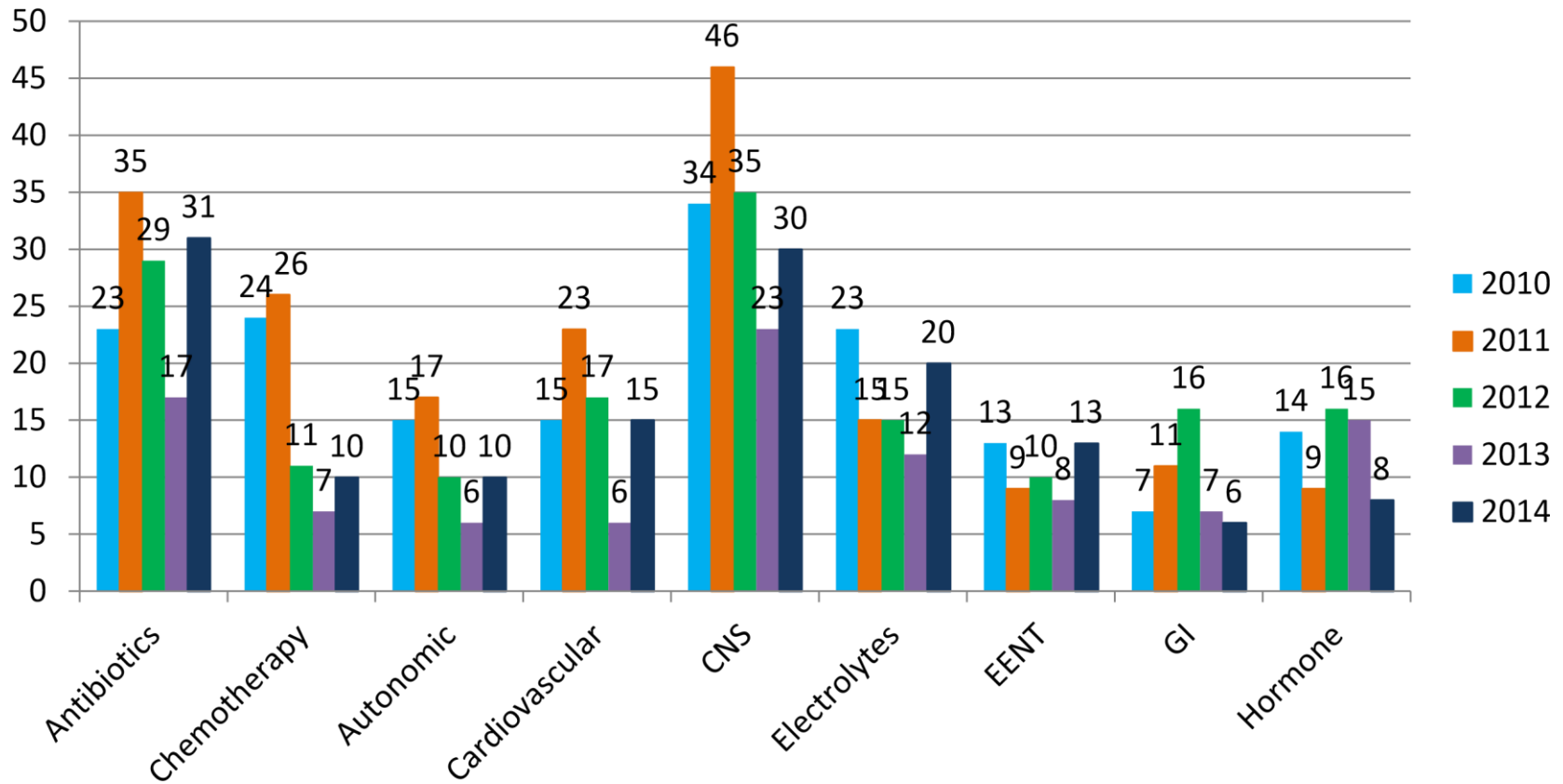


National Drug Shortages: Active Shortages by Quarter October 1, 2012 to June 30, 2018

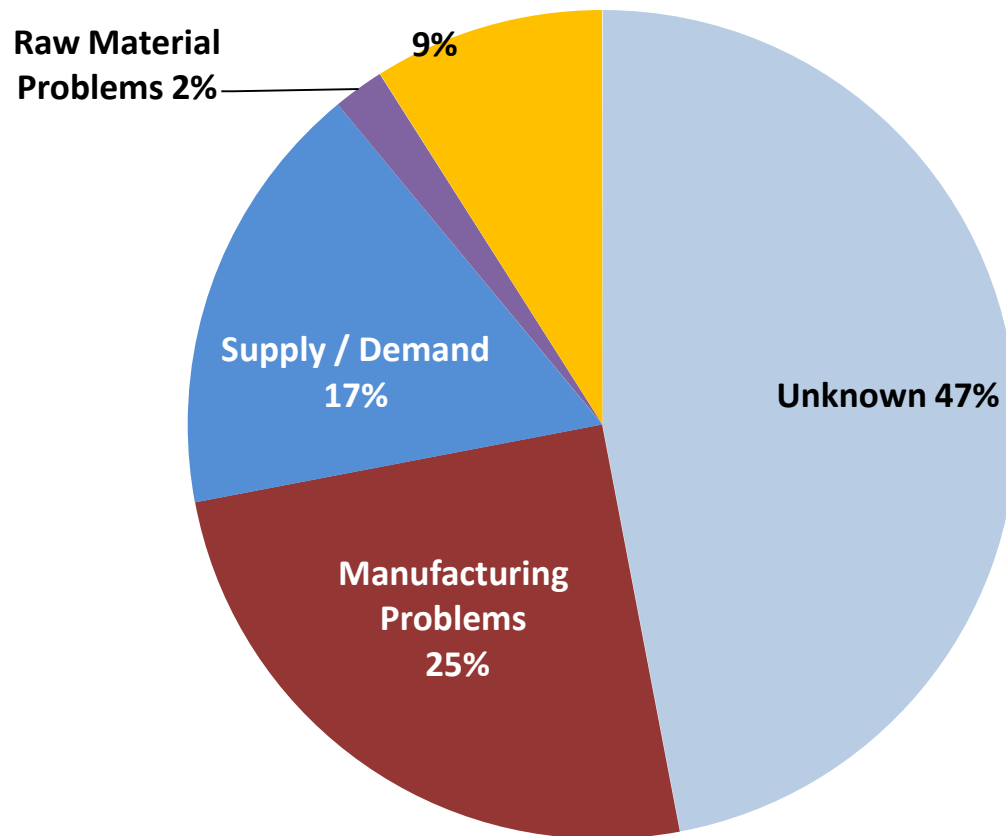


Common Drug Classes in Short Supply

New Shortages Reported: 2010 - 2014

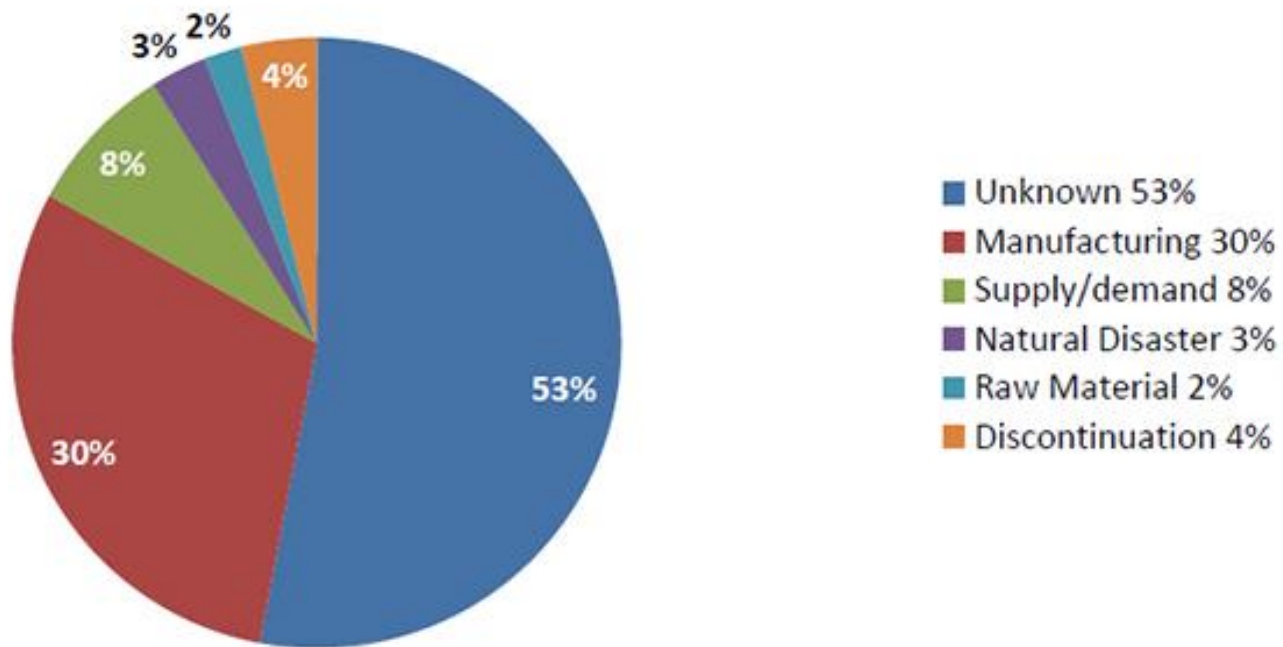


Reasons for Shortages * - Business decision / Discontinued



*Based on information provided by manufacturers to the University of Utah Drug Information Service

National Drug Shortages Reasons for Shortages -- 2017

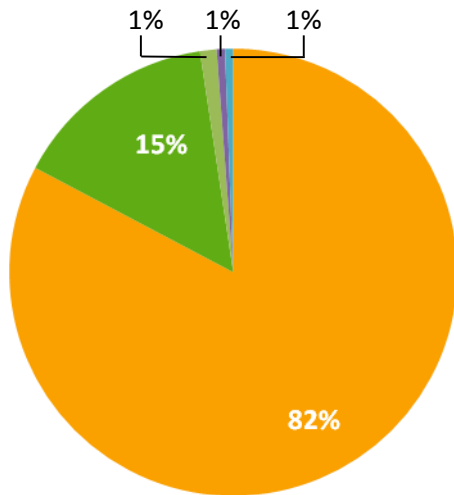


Alternative Drug Dosage Formulations

- Parenteral Dosage – “Pertaining to a medication administered by a route that bypasses the digestive tract, such as a drug given by injection” – *Mosby’s Medical, Nursing, & Allied Health Dictionary*, 5th edition, 1998
- The “5i” Drugs – Medicines administered via inhalation, infusion, instilled, implanted or injectable means

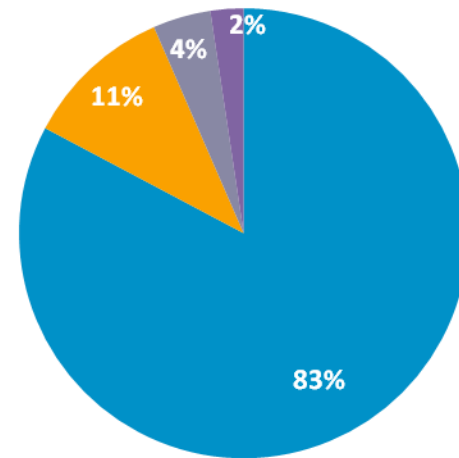
Most products are injectables and multi-sourced generics

Form Type



- Injectables
- Orals
- Inserts/Implants
- Dermatologicals
- Rectals, Topical

Brand-Generic Type

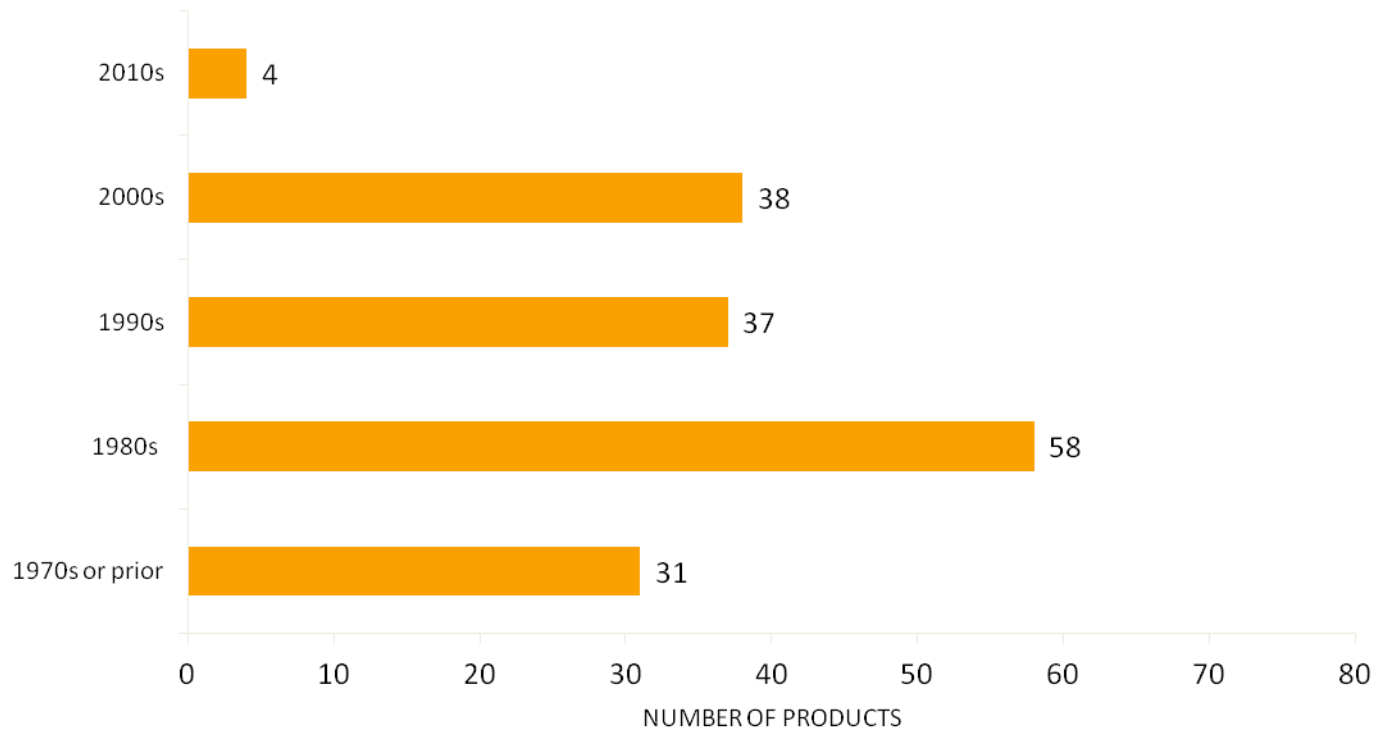


- Generic
- Brand
- Branded Generic
- Other-Branded Generic

Source: IMS National Sales Perspectives, Sep 2006 – Aug 2011

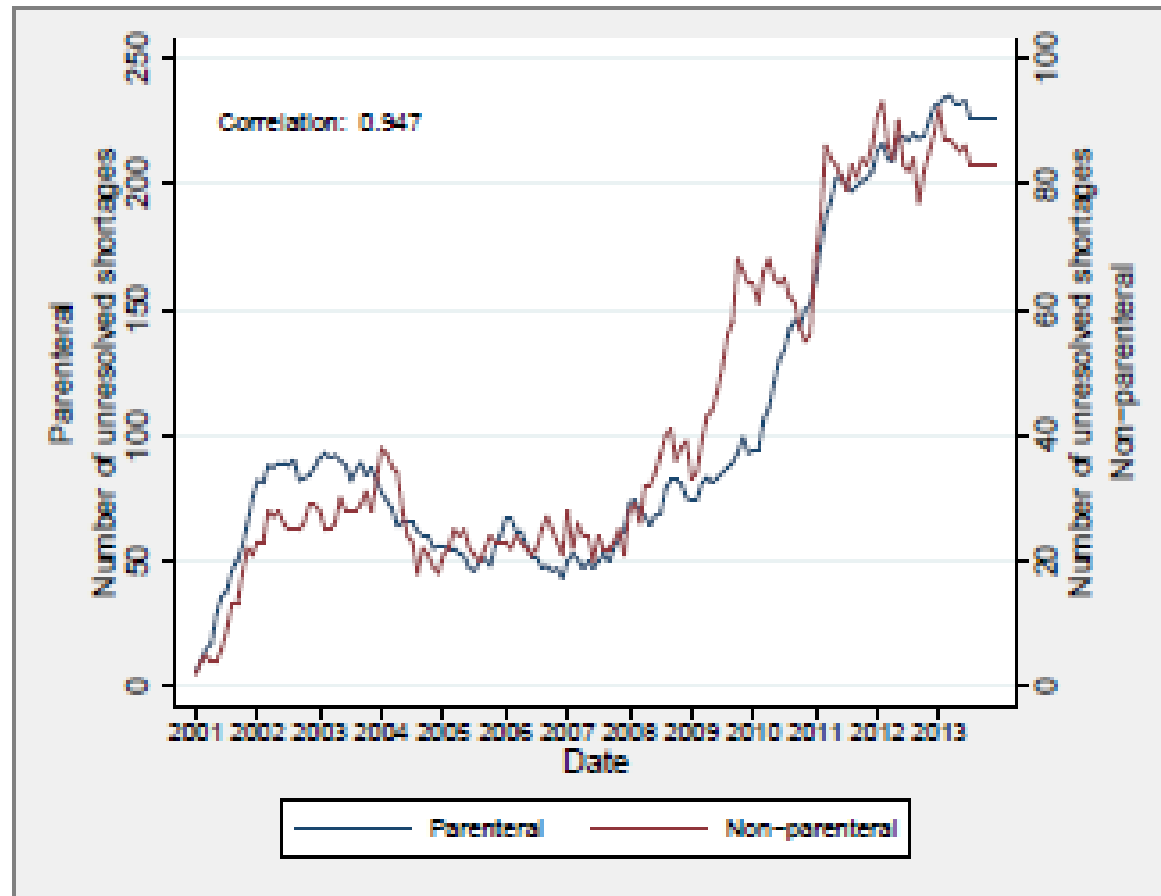
Shorted products were introduced over several decades

Decade of Product Introduction



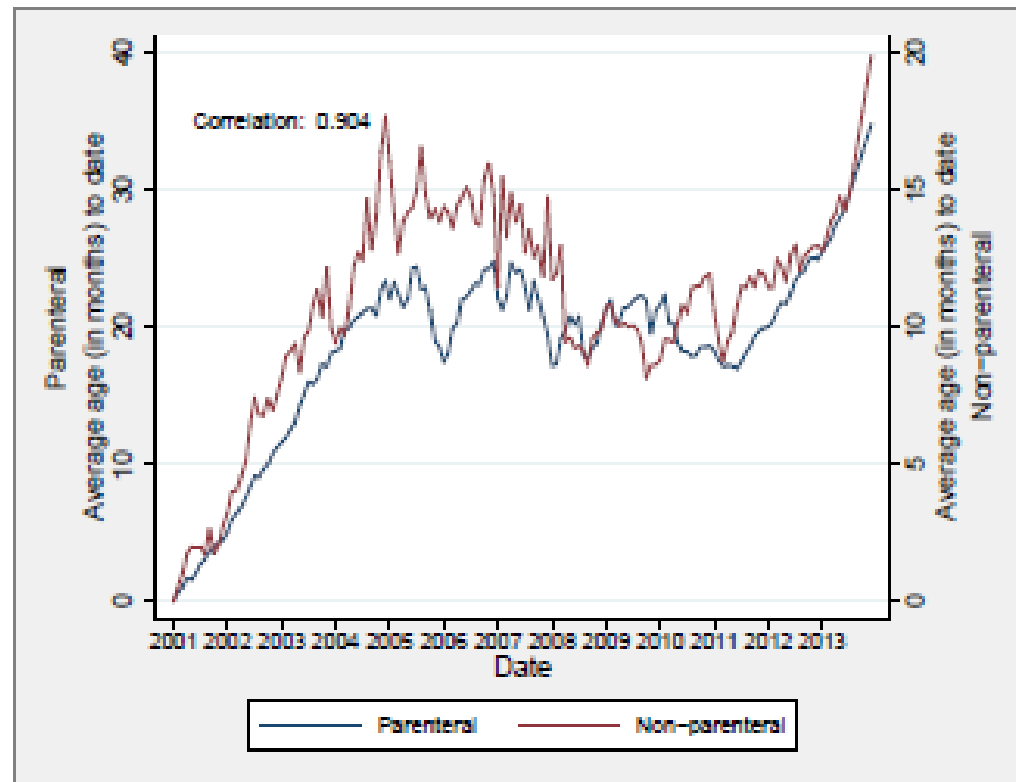
Source: IMS National Sales Perspectives, Sep 2006 – Aug 2011

Correlated Patterns of Unresolved Shortages



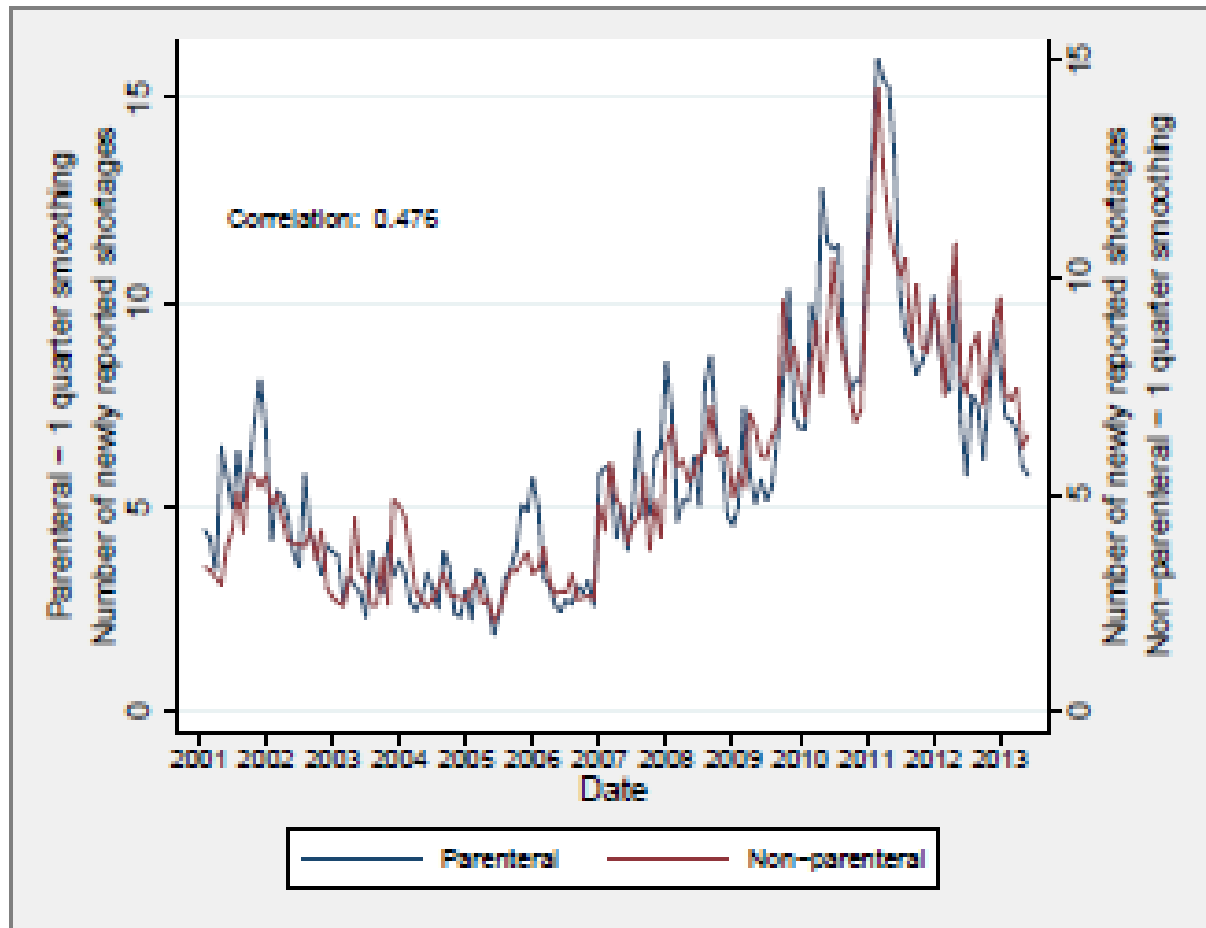
Source: American Society of Health-System Pharmacists (ASHP). Vertical axis measures the number of drugs (typically molecule-form combinations) reported to be in ongoing shortage during that month.

Average Age of Unresolved Shortages



Source: American Society of Health-System Pharmacists (ASHP). Vertical axis measures the average age (in months) of drugs reported to be in ongoing shortage during that month. Note that early-period data are truncated on the left, and thus do not accurately reflect the actual length of shortages in progress at the time the database was initially constructed.

Number Newly Reported Shortages



Source: American Society of Health-System Pharmacists (ASHP). Vertical axis measures the monthly number of newly reported drugs in shortage smoothed using a quarterly moving average (current month plus previous two months).

What's New re “Classic” Drug Shortages?

- Have had shortages in the past – flu vaccines, other vaccines, blood serum and plasma supplies (e.g., heparin), manufacturing problems – usually subside in 12-24 months
- Differences: (i) many therapeutic categories today, not localized; (ii) confined largely to US; (iii) persistent – going back to 2006-7; (iv) not decreasing in prevalence over time; (v) mostly generic “commodity” old drugs manufactured by a small number of large multiproduct generic firms; (vi) mostly infused/injected, reimbursed by Medicare Part B, administered in community office practices or hospitals
- Mystery: Why increased shortages for the non-parenteral drugs (although shortages are resolved more quickly than with parenterals)?

What's Different About Injectables? I

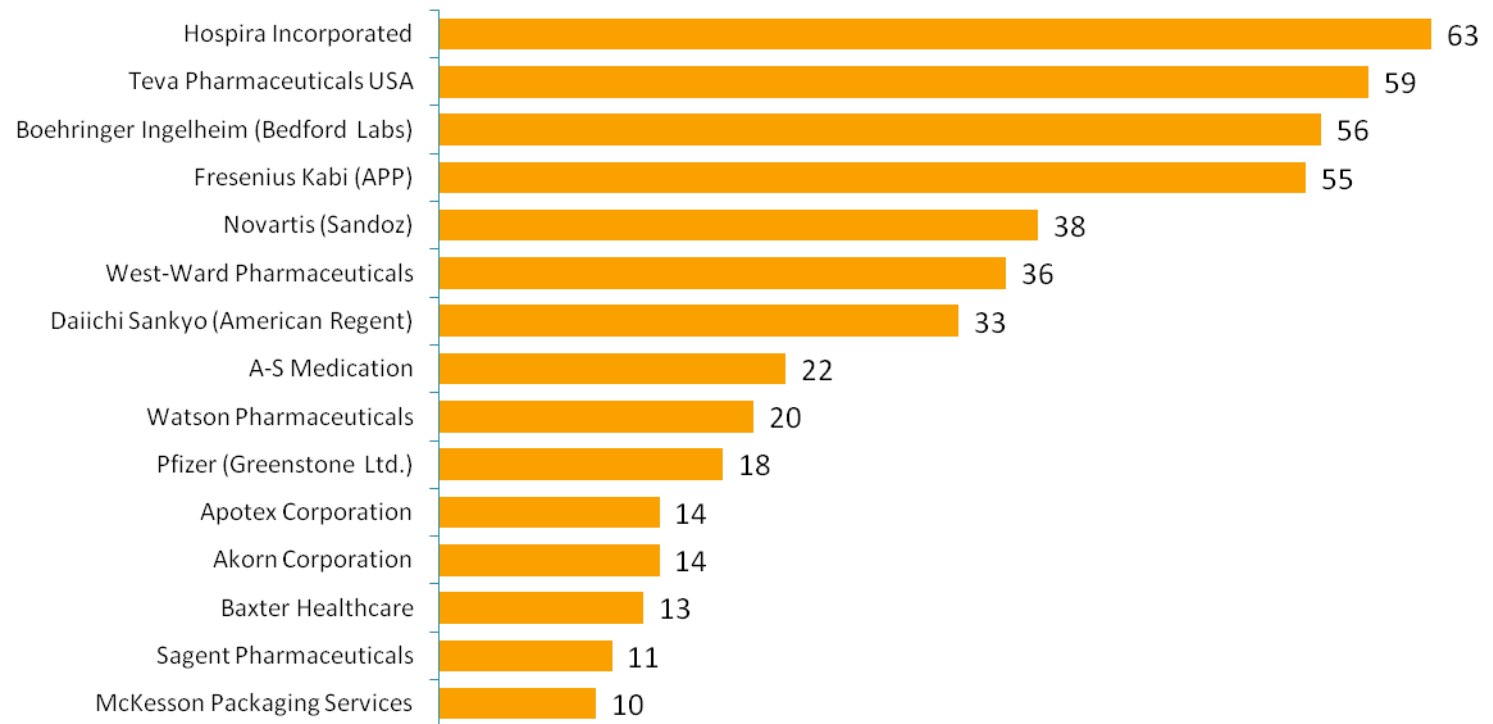
- More difficult and costly to manufacture, need aseptic “clean room” for “fill and finish” of API into sterile syringes or vials
- Need more rigorous process controls and monitoring, highly trained and re-certified work force – FDA needs to inspect processes and approve specific vats and batches
- Also need to control downstream distribution system – robust to spilling or breaking, temperature changes and light conditions – ship to providers/wholesalers, not retailers
- Higher manufacturing/distribution entry costs of generic injectables results in less generic entry than with oral solids
- Traditionally, gross margins on mature generic injectables >> mature oral solid generics (40-50% vs. 2-5%)

What's Different About Injectables? II

- Fixed costs relatively important – Injectable fill and finish increasingly automated, limiting human interactions to highly trained labor. High fixed costs generates *economies of scale*.
- For injectables, cost advantages to producing multiple products, exploiting shared fill and finish equipment inputs -- results in *economies of scope*.
- While economies of scale and scope are present for oral solids, they are likely considerably more important for injectables

Some generic firms supply many different shorted products

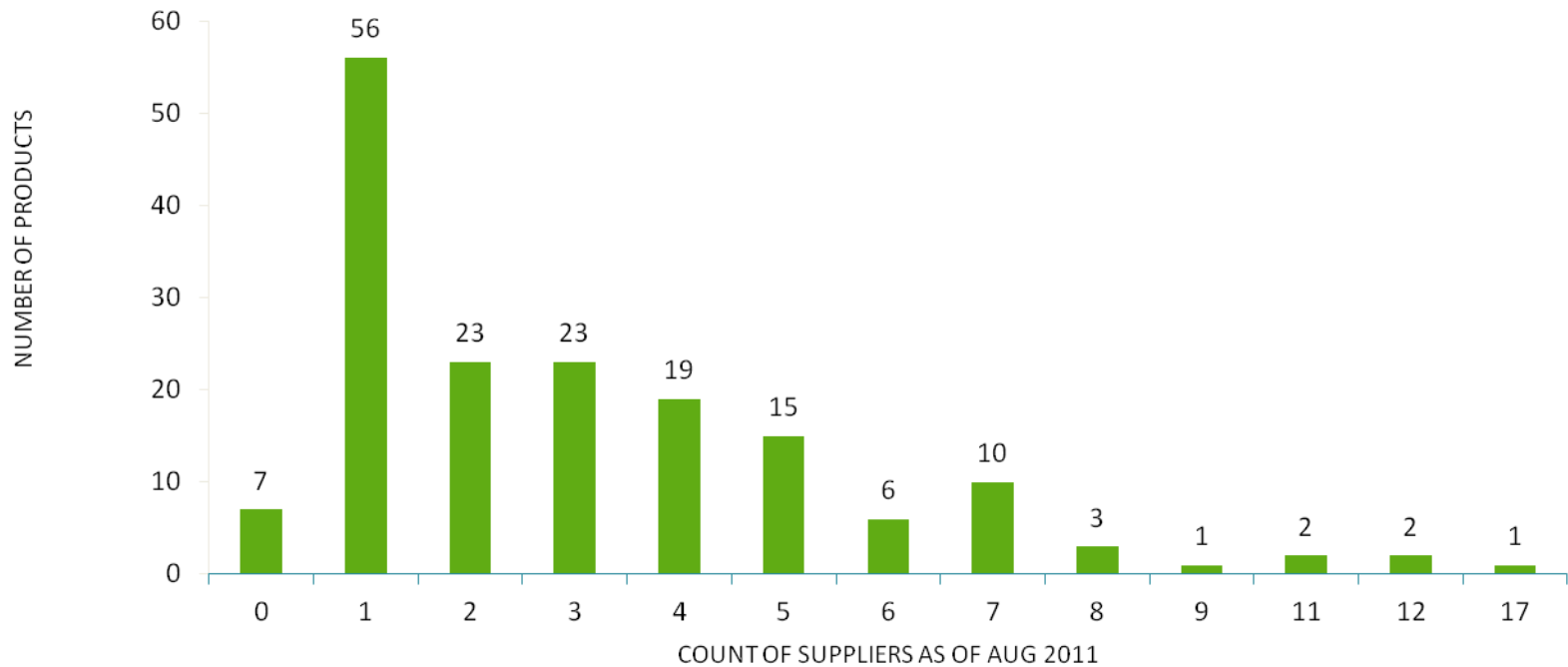
Number of Molecules by Corporation



Source: IMS National Sales Perspectives, Sep 2006 – Aug 2011

56/168 (33%) of shorted products have one supplier, two-thirds (109/168) have three or fewer suppliers

Number of Products by Supplier Count



Source: IMS National Sales Perspectives, Sep 2006 – Aug 2011

Demand Changes

- As baby boomers now retire, there's been growth in Medicare Part B population
- Recession in US since 2008 has resulted in growth in population served by Medicaid, also recent ACA eligibility expansion
- Combination of reduced reimbursement by Part B and growth of Medicaid implies drug manufacturers face a flatter government demand curve – lower quantity demanded at high prices, and greater quantity now demanded at lower prices
- Shift of care to and acquisition of community practices by hospitals – now eligible for discounted GPO and 340B prices
- Economics terminology: “Demand curve has shifted downward and to the right – demand more elastic”

Initial Observations on Root Causes of “Classic” Drug Shortages

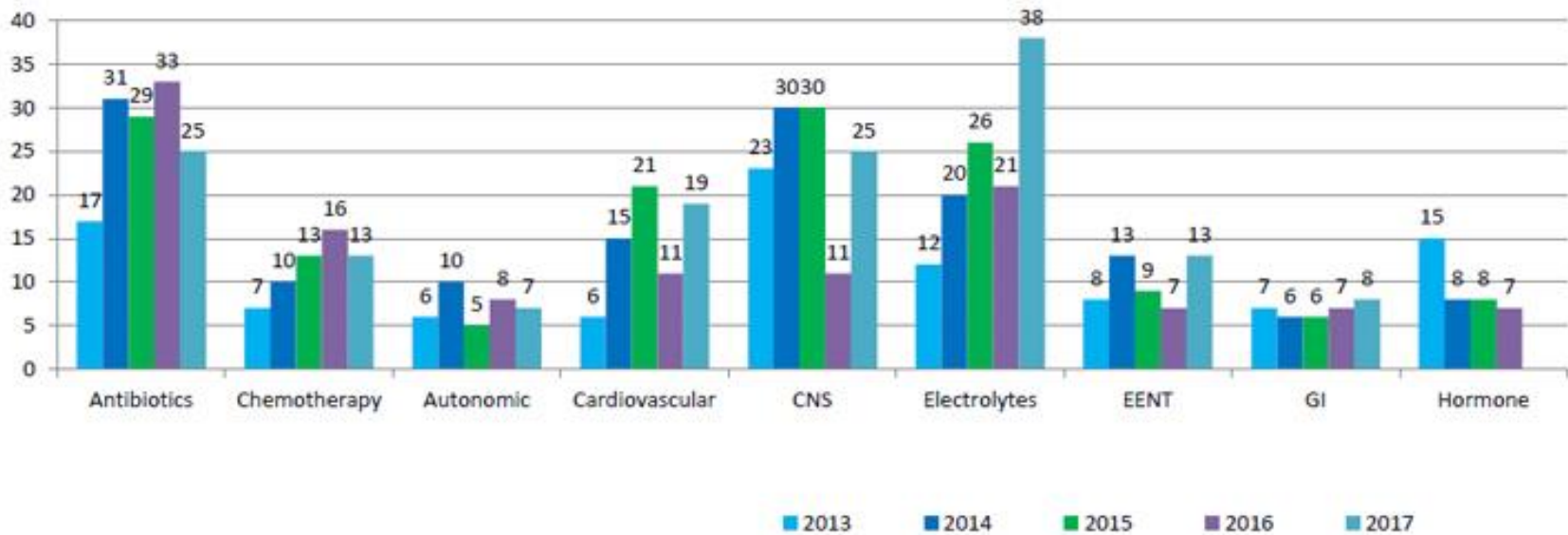
- Likely something about the demand, supply and/or pricing of these “medically necessary” drugs that does not allow the US market to “adjust” or “equilibrate” quickly to these “classic” drug shortages.
- Systemic supply side sources could be inducing low quality commitments from manufacturers, decreases in their number, and in the maintenance of their manufacturing capacity
- On demand side, greater demand price sensitivity makes investment in updated 5i capacity less attractive
- In addition, given substantial M&A activity among generic firms, incentives to unload redundant manufacturing capacity exist rather than to invest anew

Shortages Emanating from Natural Disasters

- September 2017 Hurricane Maria struck Puerto Rico, which houses significant drug manufacturing infrastructure
- Has resulted in shortages of small-volume parenteral (SVP) solution products, including saline bags (heavily used to compound drugs needing further dilution – e.g., antibiotics, chemotherapies, electrolytes – also used to start IV lines or administer blood)
- Although Section 503B of 2013 FD&C Act enabled firms to compound drugs, 503B firms simply cannot make SVP solutions because the majority of empty bags needed to do so are manufactured in Puerto Rico (see <https://www.ashp.org/Drug-Shortages-Resources-Report> for more details)

National Drug Shortages: Common Drug Classes in Short Supply

New Shortages Reported: 2013-2017



“Classic” vs. “Disaster” Shortages: Different Issues and Different Solutions? Some Preliminary Thoughts

- “Classic” shortages seem to have systemic underlying supply and demand issues requiring data-informed non-transitory changes in reimbursement policies and investment and regulatory incentives
- In contrast, shortages emanating from “disasters” raise issues of restoring manufacturing and distribution capacity, and maintaining inventories of “medically necessary” products (akin to Strategic Petroleum Reserve?)
- As the UK prepares for a possible March 2019 “Brexit” divorce, both public and private sectors are making and beginning to implement plans to avoid drug shortages – are these “Brexit” shortages a hybrid of “classic” and “disaster” shortages?
- Regardless, in all three shortage types, management and prevention requires public access to manufacturing data