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Boston Medical Center  
**HEALTH SYSTEM**

# Breaking Even During Price Hikes in the Intensive Care Unit

A HealthTrust Member Webinar  
May 8, 2018

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## Disclosures

- This program may contain the mention of drugs or brands presented in a case study or comparative format using evidence-based research. Such examples are intended for educational and informational purposes and should not be perceived as an endorsement of any particular supplier, brand or drug.
- The presenters have no financial relationships with any commercial interests pertinent to this presentation.



# Learning Objectives – PharmDs & Nurses

- Describe the impact of recent prescription medication price hikes
- Discuss the use of improvement science to break even during the intravenous acetaminophen, sodium nitroprusside, vasopressin and pyrimethamine price hikes
- Identify lessons learned and proactive approaches to overcome future drug pricing challenges

# Learning Objectives – Pharmacy Techs

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- Recall the impact of recent prescription medication price hikes
- Discuss inventory management strategies for combating price hikes
- Identify lessons learned from Boston Medical Center in overcoming drug pricing challenges

# Boston Medical Center



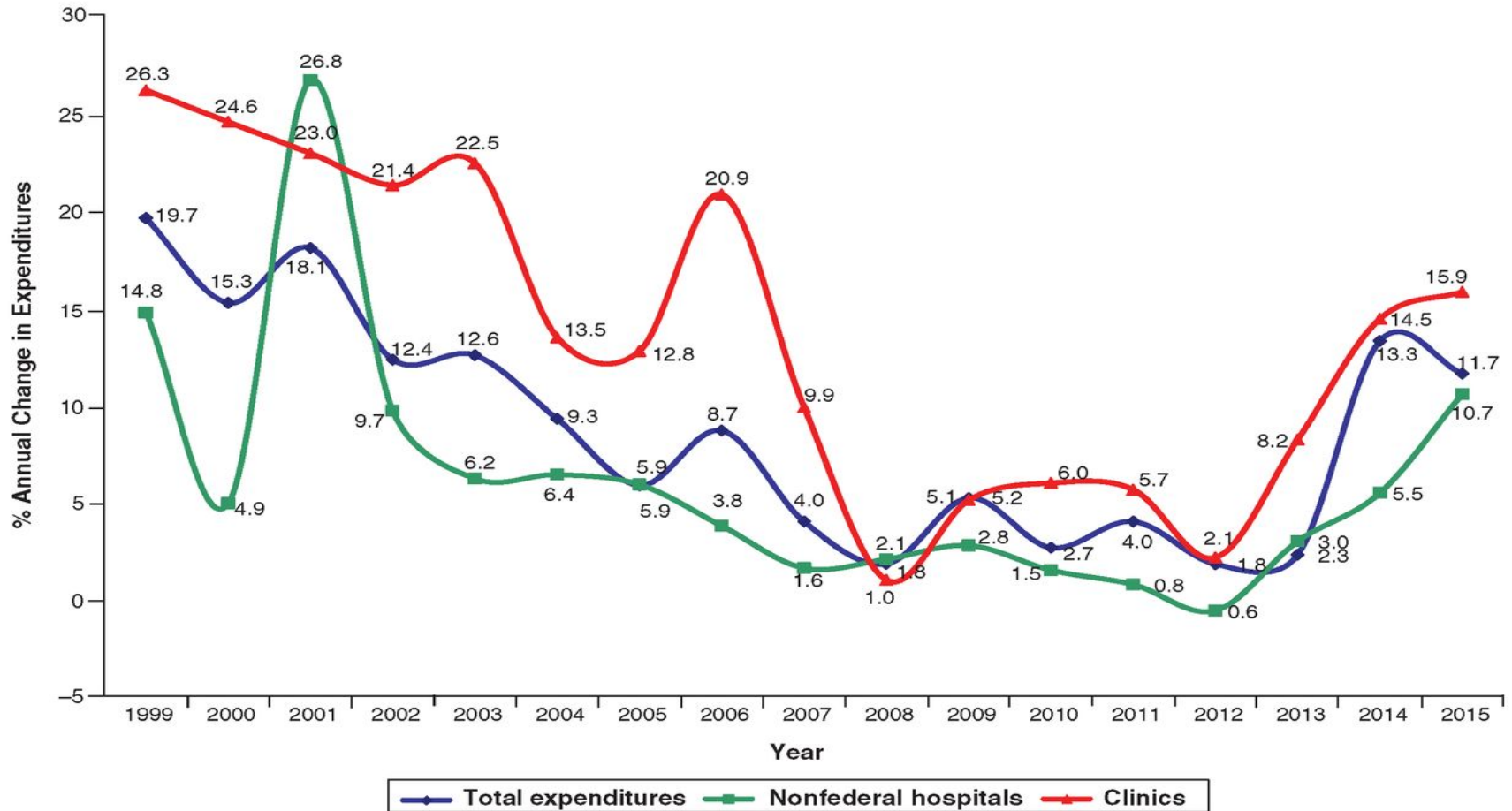
- Fiscal Year 2017 Statistics
  - 567 Beds
  - 25,840 Inpatient Admissions
  - 133,529 ED Visits
- Patient Population
  - 57% under-served
  - 32% do not speak English as first language
- Largest safety net hospital in New England

# Outline

- Briefly describe what we see
  - Why is this happening?
    - Regulatory Environment
    - Market Factors
    - Drug Shortages
  - Literature reported strategies
- Case examples using improvement science
- Lessons learned and developed tools



# Prescription Expenditure Trends



# Drug Cost Drivers

Product Category	Clinics				Nonfederal Hospitals			
	Total Percent Growth	Percent Growth Due to Factor			Total Percent Growth	Percent Growth Due to Factor		
		New Products	Price	Volume and Mix		New Products	Price	Volume and Mix
All products	15.9	3.1	3.8	9	10.7	2.6	7.6	0.5
Injectables	13.9	2	3.4	8.5	11.3	2.4	7.3	1.6
Brands	13.9	1.8	3.6	8.5	8.6	1.2	4.2	3.1
Generics	7.3	4.4	-1.7	4.6	16.5	9.1	6.4	1
Branded generics	20.3	1.7	6.2	13	19.5	0.3	25.7	-6.4
Noninjectables	23.3	7.2	5.3	11	9.2	3.4	8.4	-2.6
Brands	26.4	7.9	6.4	12	10.4	3.3	11.4	-4.3
Generics	19.5	8.3	-1.0	12	15.2	7.4	5.2	2.5
Branded generics	8.1	0.8	6.8	0.5	1.7	0.1	6.8	-5.3



# Drug Cost Drivers

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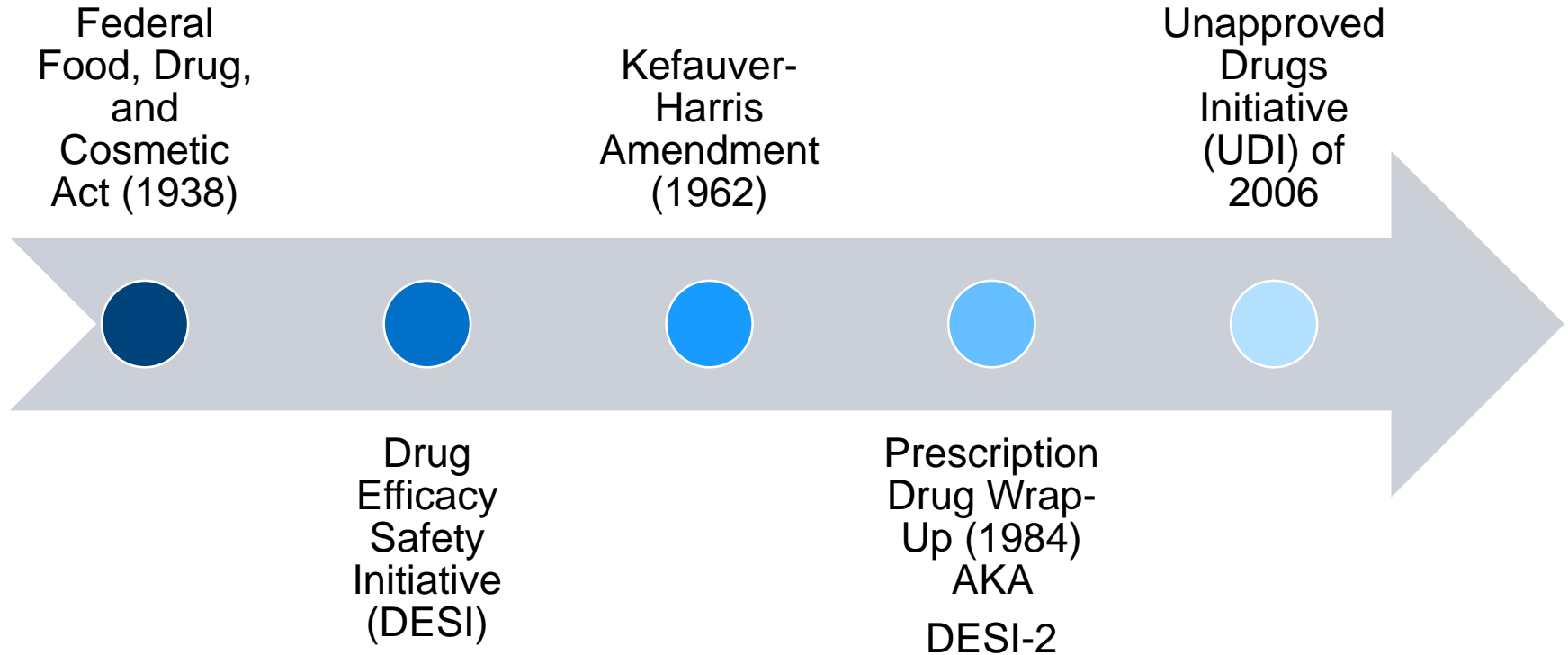
# Why the Concern?

- Unprecedented healthcare spend
  - Drug spend continues to significantly outpace inflation
- Limited resources, high focus cost center
- Disproportionally increased spend
  - Specialty drugs
  - Branded small molecule drugs
  - Generic drugs with recent significant percent increases

Source: Centers for Medicare and Medicaid Services. National health expenditures 2014 highlights. [www.cms.gov/Research- Statistics-Data-and-Systems/Statistics-Trends-and-Reports/ NationalHealthExpendData/Downloads/highlights.pdf](http://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/Downloads/highlights.pdf)

# Regulatory Environment

# FDA and Unapproved Drugs



# Unapproved Drug Initiative

## Intent

- Modernize safety/efficacy, Good Manufacturing Practices (GMP)
- ~5000 drugs affected
- Once approved, market exclusivity granted

## Effect

- FDA does not consider cost when approving or granting exclusivity
  - Up to three years exclusivity for the original indication
  - Up to seven years exclusivity under the Orphan Drug Act
  - Prices rose exponentially
  - Drug Shortages

# \*UDI Ex: Colchicine

- Ancient drug
- No prior review under amendments
- Labeling vague, little oversight
- Narrow therapeutic index, high patient variability
- Reported: 117 deaths
- Review/Approval
  - Granted 3 years exclusivity for Gout
  - Granted 7 years exclusivity for Familial Mediterranean Fever
- Price/Cost Differential
  - Price per tab: \$0.09 → \$4.85
  - Medicare/Medicaid Cost: \$1M → \$50M

# Market Economics



# Generic Manufacturers

- Under Hatch-Waxman Act:
  - Generic manufacturers faced reduced regulatory constraint
  - Medications reduced cost in the overall market
- By 2009 the market was saturated
  - Competitive environment
  - Difficult to make a dollar
- Supply, Demand, Competition

# Re-branded Medications

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Company decides to pursue approval



Submit to FDA



Recoup investment cost through price increases

# \*\*Market Economics: Pyrimethamine

- Pyrimethamine first developed in the 1950s
  - Treats *Toxoplasma gondii* infections
  - 2005 Cost: \$70 per course
- Market Factors
  - CorePharma purchases the right to produce in 2010
  - 2010 Cost: \$900 per course
  - Turing Pharmaceuticals purchases the right to product in 2015
  - 2015 Cost: \$31,500-\$73,500 depending on patient response
- No development costs to recoup

# Drug Shortages

# Supply and Demand

- Supply
  - Fragmented
  - Inconsistent and unpredictable
- Demand
  - Generally stays consistent barring:
    - Guideline/practice changes
    - Seasonality

# Association Between Shortages and Price Hikes

Medication	Drug Shortage Period	% AWP Increase During Shortage
Ephedrine	Mar 2014-Oct 2015	690
Furosemide inj.	May 2010-May 2016	56-128
Glycopyrrolate inj.	Jan 2011- Mar 2015	633-2278
Hydralazine inj.	Sep 2014-May 2016	921
Ketorolac	Nov 2009-May 2016	251
Magnesium sulfate	Mar 2011-Nov 2015	49-120
Sodium phosphate	Dec 2012-Aug 2015	2220

# Strategies

- Manage dispensing through systems
- Centralize stock and evaluate operational efficiencies
- Med Use Evaluations: Evaluate the literature against practice
- Evaluate contract opportunities
- Compound oral preparations



# Assessment Question #1

Which of the following best represents the root cause for increased drug cost during the last three budget cycles?

- A. Truly generic oral tablets
- B. Re-branded injectable drugs
- C. Truly generic oral capsules
- D. Truly generic injectable drugs

# Response Question #1

Which of the following best represents the root cause for increased drug cost during the last three budget cycles?

- A. Truly generic oral tablets
- B. Re-branded injectable drugs**
- C. Truly generic oral capsules
- D. Truly generic injectable drugs

# Summary – Part 1

- Changes in FDA regulations and initiatives have increased cost to manufacturers
- In a capitalistic economy, profit drives private companies
- Competition is a balance
- The results have created increased costs in drug with little to no added benefit nor knowledge to the medical community

# Dollars and Sense in the ICU

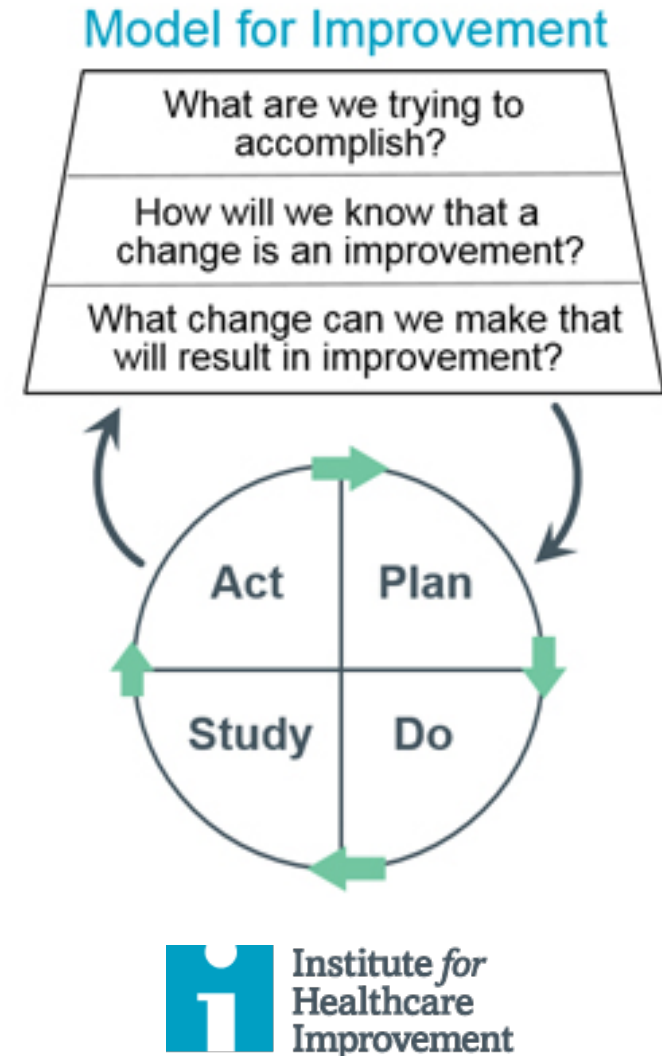
- Different cost-related challenges
  - Cost increases by 5-50 fold over 1 year
    - Vasopressin, norepinephrine, isoproterenol, calcitonin, ethacrynic acid, chlorothiazide
  - Usual suspects
    - MDIs, inhaled nitrous oxide/epoprostenol, dexmedetomidine, rhVIIa, PCC, albumin
- Unknown clinical impact
  - Local survey of critical care pharmacists (n=36 New England hospitals) → less likely to recommend vasopressin due to increasing cost
  - Norepinephrine use decreased by 20% across 26 hospitals during a 2011 shortage → 3.7% increase in absolute risk of death (NNT 27)

# Application of Improvement Science to Price Hikes

- Right tools for the job
  - Align projects with department and institutional goals
- New ASHP residency standards embrace QI
  - PGY1 – Goal R2.2: Demonstrate ability to evaluate and investigate practice, review data, and assimilate scientific evidence to improve patient care and/or the medication-use system.
  - PGY2 CC – Goal R2.2: Demonstrate ability to conduct a quality improvement or research project.
- Develop new knowledge and skills
  - Lean, six sigma for operations
  - Institute for Healthcare Improvement for clinical initiatives

# Application of Improvement Science to Price Hikes

- Set an aim
  - How good? For whom? By when?
- Build a team
- Describe the problem
  - Focus on local problem
  - Develop cause-and-effect and driver diagrams, current vs. ideal process maps
- Identify and implement interventions through small tests of change on your ICU patients
  - Learn from and share your experience
- Identify outcome, process, and balancing metrics
  - (Generally) no IRB → collect your own data, plot over time



# Local Context for Surgery ICU Price Hikes

- Surgery services
  - Trauma and acute care, bariatric, colorectal, otolaryngology, cardiac, thoracic, vascular, orthopedic, neuro, urology, and plastics
- Medicine, ICU-focused pharmacy services
  - Trauma ICU (2004-present), surgical ICU (2012-present) including kidney transplant
  - Acute care, OR/PACU pharmacists (2017)
- Challenges with surgery
  - No clear training path for surgery pharmacists
  - Multiple teams with low census, resident/APP only rounds
  - Strong personalities, disagreements escalated to director
  - Perceive pharmacy as barrier to care, cost first



# Should You Add IV Acetaminophen to Formulary?

- Shift away from opioids as first-line towards adjuncts
  - Fast-track, enhanced recovery protocols emphasize reductions in opioids
  - 5.9-6.5% of patients newly prescribed opioids chronically after surgery
  - Advance directives can exclude opioids
- Limited IV options
  - Pain reduction by 50% over 4 hours
    - IV x1 = 36%, placebo = 16% (NNT 5)
  - Inconsistent impact on opioid use and opioid-related side effects, outcomes
    - Patients and providers tell a different story

Source: *JAMA Surg* 2017;152(3):292-8. *JAMA Surg* doi:10.1001/jamasurg.2017.0504 [www.statnews.com/2017/03/19/opioid-prescription-refuse/](http://www.statnews.com/2017/03/19/opioid-prescription-refuse/) *Cochrane Database Syst Rev* 2016;23(5):CD007126. *Pharmacotherapy* 2012;32(6):559–79. *J Healthc Qual* 2015;37(3):155-62

# IV Acetaminophen Timeline at BMC

Date	Event
Jun 2012	2 <sup>nd</sup> request for addition to formulary → accepted with stringent prescribing restrictions: 1) NPO/NPR and 2) limited to PONV, neurologic injuries, or ileus. Anesthesia approval needed for >24h duration.
Nov 2013	MUE showed 90% adherence to criteria, projected \$14K annual expenditure
Feb-Mar 2014	Mallinckrodt Pharmaceuticals acquires IV acetaminophen Revised prescribing restrictions to be less stringent: change to 48h initial default duration, added to IV-to-PO pharmacist conversion policy, pharmacist approval for therapy >48h
May 2014	Transition to new EHR, added to all post-op order sets
Sep 2014	Approximately \$55K spend in August 2014 and projected \$540K spend in fiscal year 2015 → QI team

# IV Acetaminophen QI Project Methods

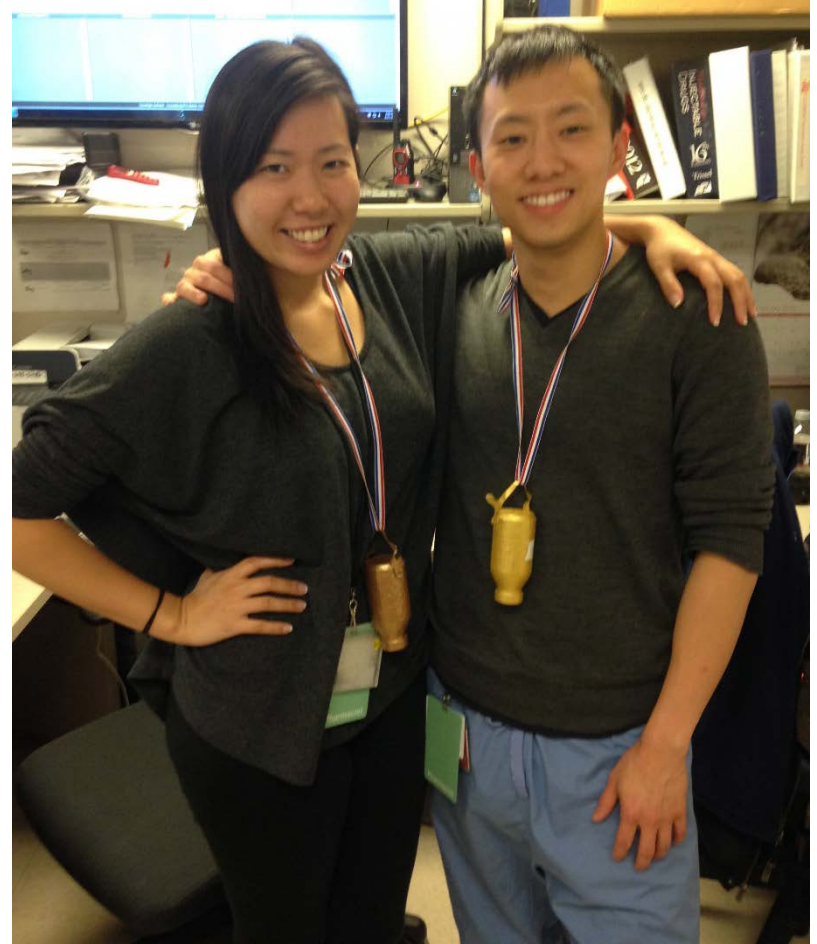
## Interventions

- PGY1 resident outcome-based, IRB-approved research project (Jul 2014)
  - Less opioids but no impact on outcomes
- Short-cycle pharmacy initiative to improve adherence to prescribing restrictions (Dec 2014-Feb 2015)
- Revised prescribing restrictions via order set only, ERAS protocol implementation (Fall 2015)
  - 1 dose only, service limits, attending approval for >1 dose.

## Tools

- Asana™ for project and task management
  - Track timeline, feedback
- Access to real-time use and dispensing data
  - IV room doses prepared
  - Automated dispensing cabinet doses dispensed
  - Doses administered
  - Interventions
  - Cost from wholesaler
- QI macro for MS Excel™
  - Create run and statistical process control charts

# IV Acetaminophen QI Champions



# Information Systems Interventions

Order Sets

▼ IV acetaminophen Manage My Version▼

Medication

▼ One post-operative dose - no approval required

☐ 1000mg IV acetaminophen x1

☐ 1000mg IV acetaminophen x1 followed by PO liquid 975mg q6h

☐ 1000mg IV acetaminophen x1 followed by PO tablets 975mg q6h

☐ 1000mg IV acetaminophen x1 followed by PO liquid 975mg q6hPRN

☐ 1000mg IV acetaminophen x1 followed by PO tablets 975mg q6hPRN

▼ Use beyond one post-operative dose - requires attending approval

☐ acetaminophen IV

1,000 mg, Intravenous, Every 6 hours, for 24 hours

Intervention

Type  
**Restricted Medications**

Subtype  
IV acetaminophen

Status  
Open

Significance  
Low

Value

Time spent Response Outcomes

Associated Orders

acetaminophen IV 1,000 mg

Order Name or ID

Associated Users

Scratch Notes

Documentation

★ | B | D | ? | + Insert SmartText

**Restricted Medication Request**

Acetaminophen 1000 mg IV q6h around-the-clock was Approved for 24h by Dr. John Smith.

For any questions, please contact the approving provider.

Thank you,

acetaminophen IV 1,000 mg

✓ Accept ✗ Cancel

Order Inst.: Restricted to one postop dose per pt after general surgery, trauma and acute care surgery, or cardiothoracic surgery if NPO. Use beyond one dose for these pts requires attending approval by phone to central pharmacy on Menino 4-7687 or East Newton 8-6784. For pts < 50 kg, dose = 15 mg/kg, max 75 mg/kg/day or 3750 mg/day. For pts ≥ 50 kg, max 1000 mg/dose or 4000 mg/day. For more information, please refer to the adult pain management medication guideline.

Reference Links: Dose: 1,000 mg 15 mg/kg 1,000 mg

Administer Dose: 1,000 mg

Administer Amount: 100 mL

Route: Intravenous

Frequency: Every 6 hours Once Q6H Q8H Q6H PRN Q8H PRN

For: 24 Doses Hours Days

Starting: 1/19/2017 Today Tomorrow At: 1300 Show Additional Options

First Dose: Today 1300 Last Dose: Tomorrow 0700 Number of doses: 4

Scheduled Times: Hide Schedule

1/19/17 1300, 1900

1/20/17 0100, 0700

Patient NPO? Yes No

Requesting Service? General Surgery Trauma Surgery Cardiothoracic Surgery Other

Requested Therapy? One dose More than one dose

Attending approval obtained? Yes No

Attending Name? Dr. Smith

Admin. Inst.: Doses of 1000 mg may be administered by inserting a vented intravenous set into a 100 mL vial (10 mg/mL) without ...

Prod. Admin. Inst.: (none)

Priority: Routine Routine

Dispense: Dispense every hours

☐ Do not dispense doses

☐ Calculate rate from volume and duration

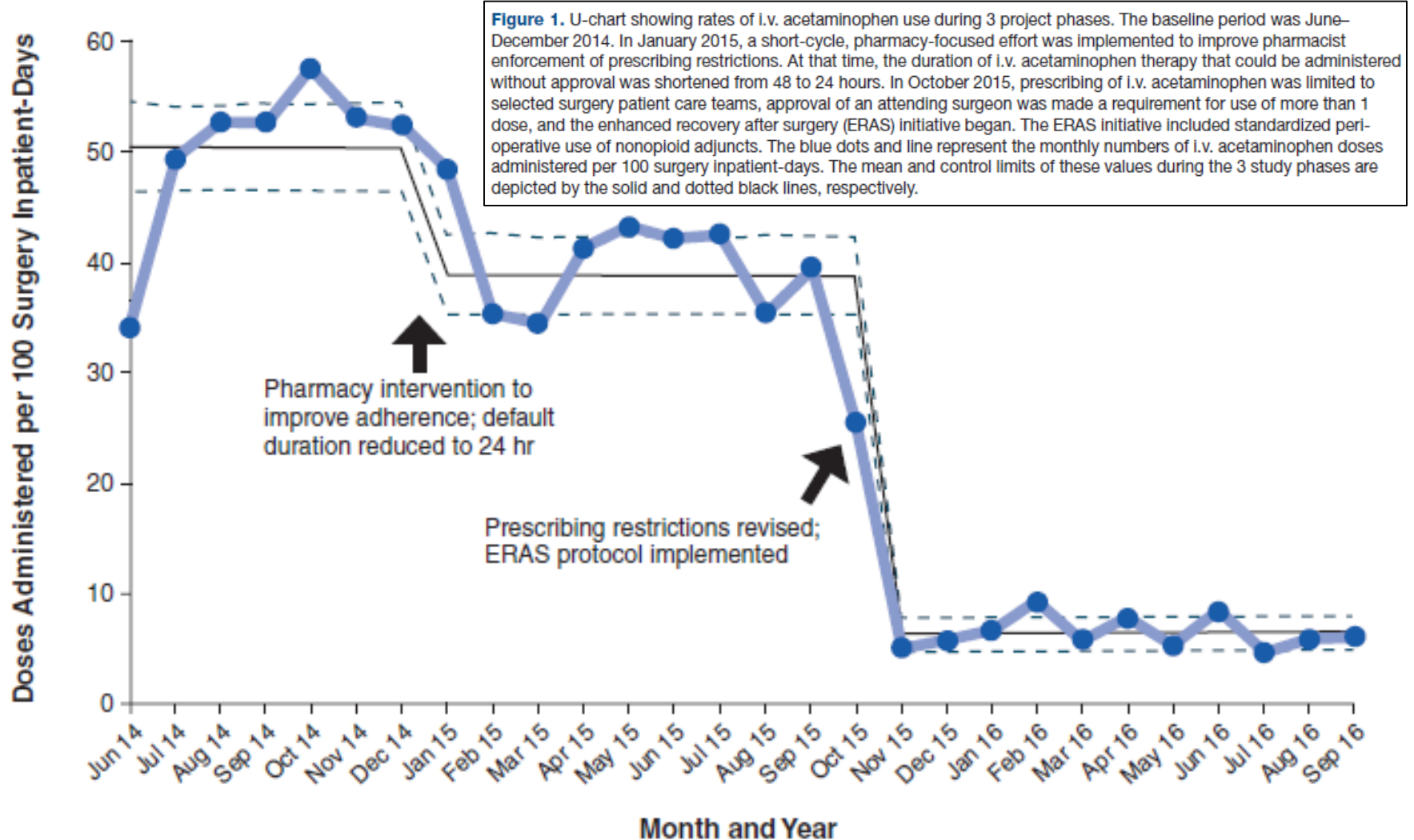
Label comments:

Additional Order Details

Next Required

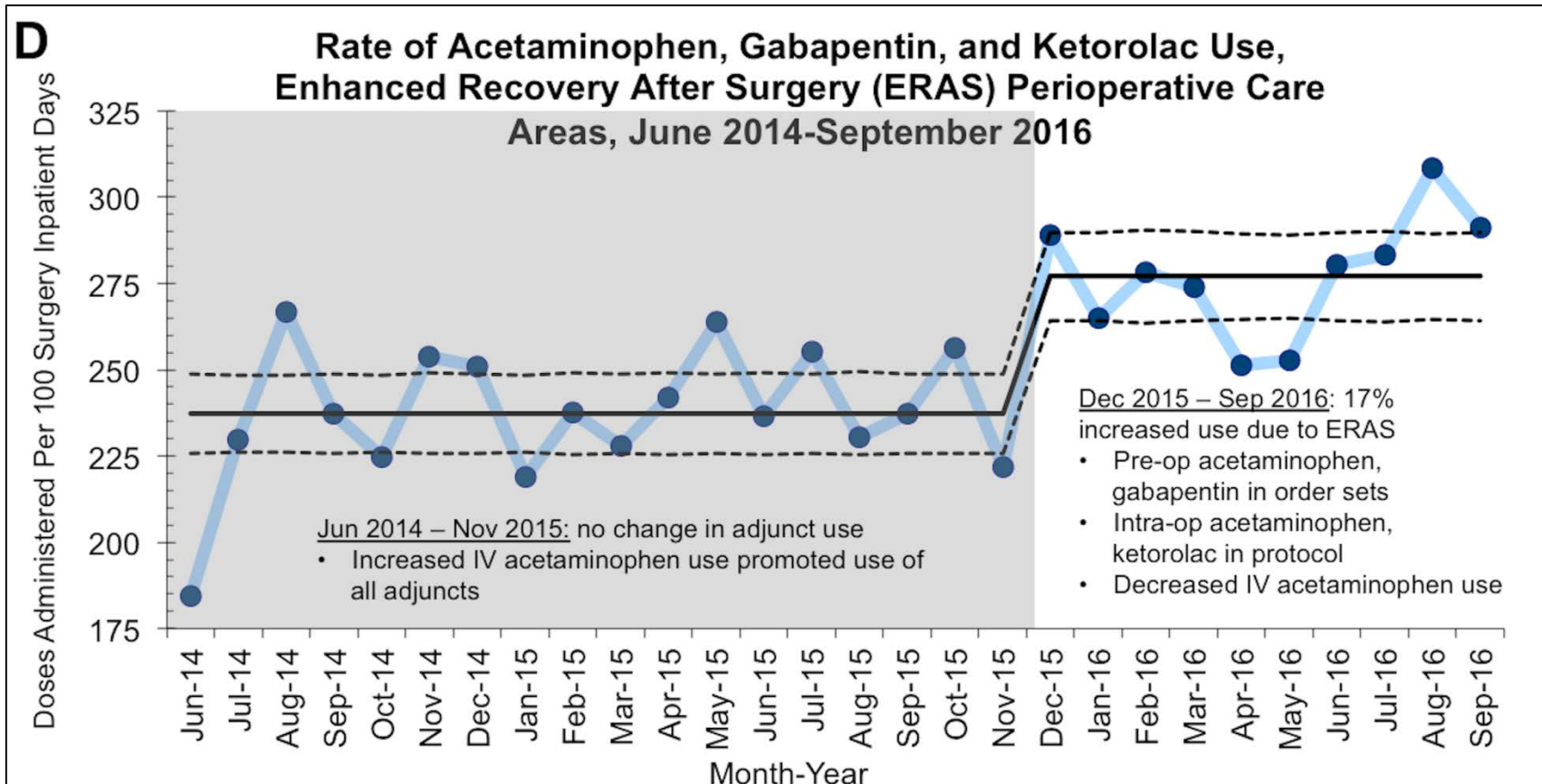
✓ Accept ✗ Cancel

# Outcome Metric – Rate of IV Acetaminophen Use (U Chart)





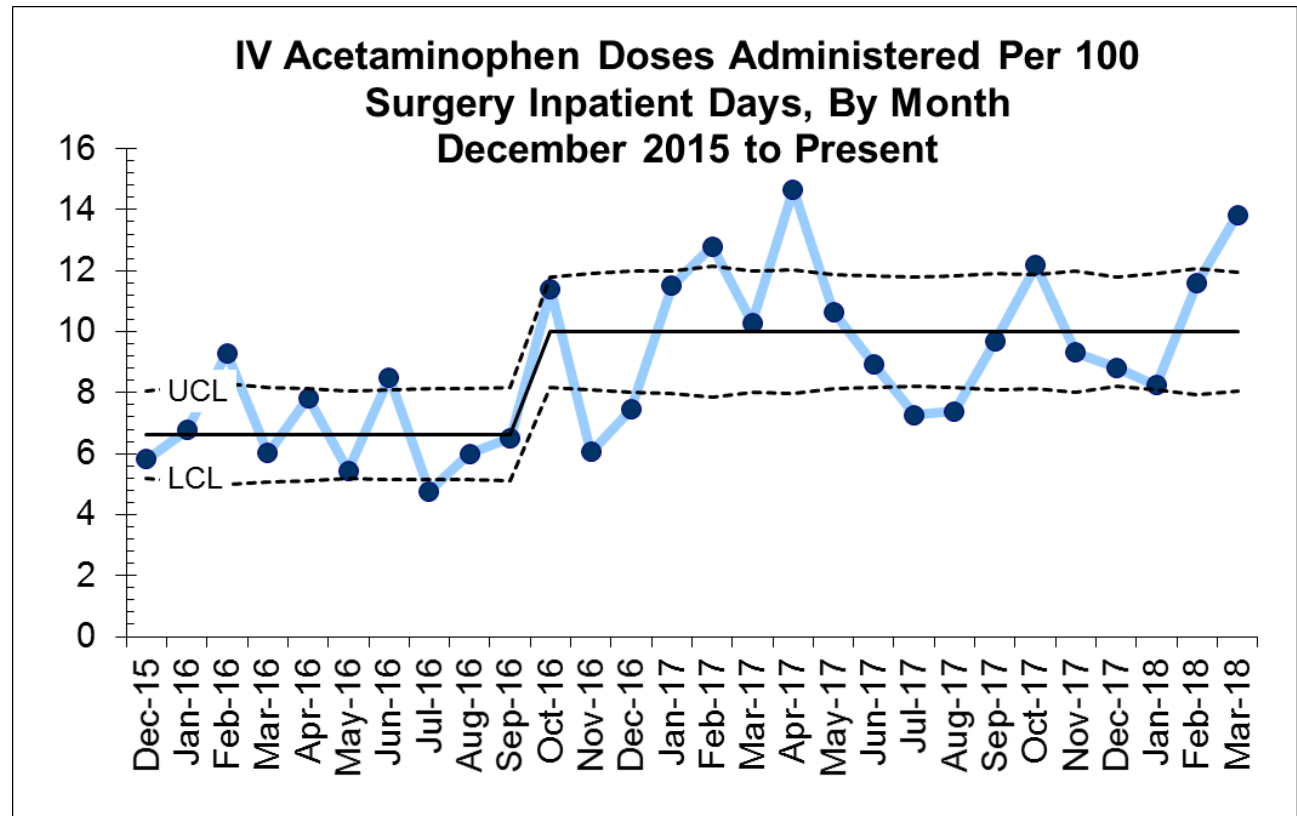
# Process/Balancing Metric – Rate of Non-Opioid Adjunct Use (U Chart)





# Sustain Success (for 2 More Years)

- Revisit eligible services/patients
  - Omits neurocritical care, septic shock
- Revisit approval process?
  - Stop calling attending surgeons for approval for > 1 dose, clarify in CPOE
  - Strict NPR
  - OR/PACU only
  - 2020 countdown



# IV Acetaminophen QI Project Summary

- Reduce IV acetaminophen annual spend to < \$100,000 in FY16
  - Short-cycle, incentivized pharmacy focus on prescribing restrictions
  - PGY1 outcomes evaluation
  - Enhanced recovery after surgery
  - Service-based, duration restrictions
- Reported data over time
  - Doses per 100 patient days, cost, interventions, all adjunct doses per 100 patient days
- Lessons learned
  - Better relationships with surgery and possibly better care
  - IHI model for improvement = tools to tackle future initiatives
  - Need to continue monitoring monthly, revisit restrictions and approval process

# Assessment Question #2

Which of the following statements about improvement science is true?

- A. All PGY-1 residents must complete research projects according to the 2015 competency areas and goals
- B. All institutions require Investigational Review Board review of quality improvement projects
- C. Pre vs. post/before vs. after analysis is the best way to demonstrate improvement
- D. Representing data over time is typically preferred over summary statistics

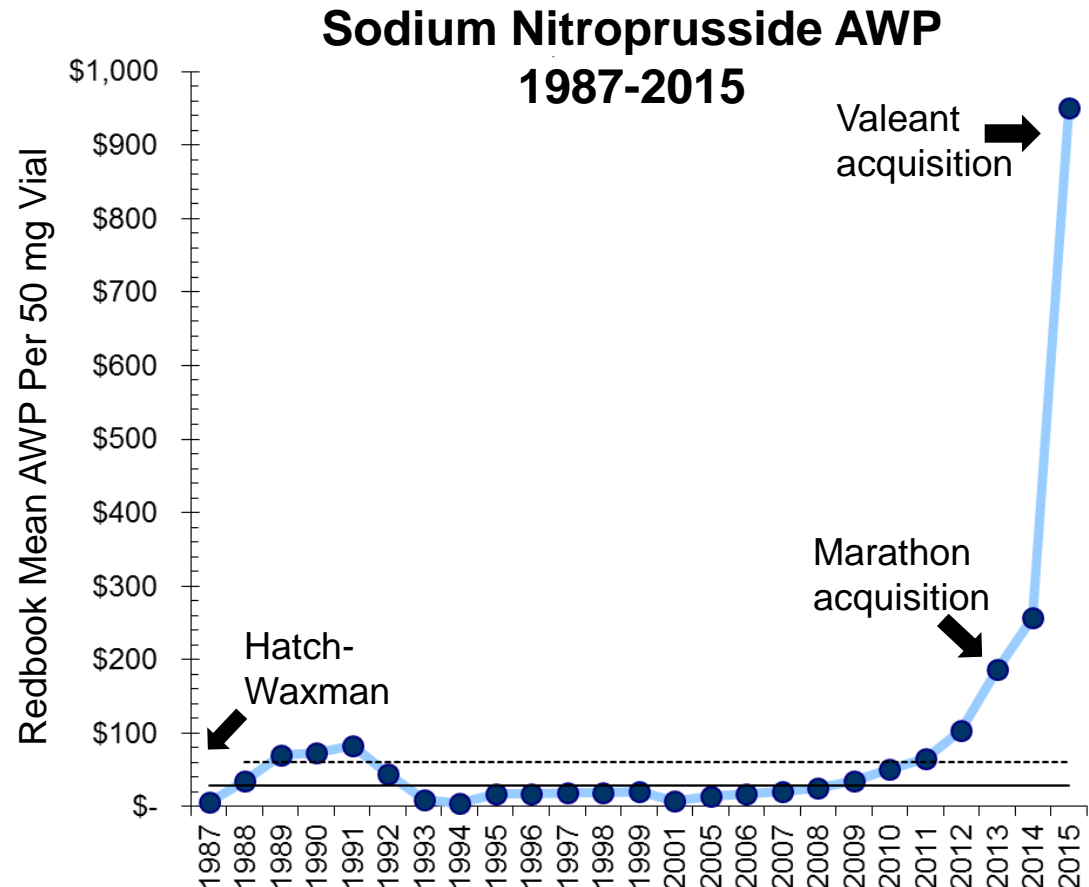
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# Sodium Nitroprusside Re-Branding

- Spring 2015
  - Purchaser:  
“Hey Will, we need to start talking about Nipride. It’s like \$800 per dose”
  - Me: “...”  
(inaudible muttering)



# The ICU Blood Pressure Players

Category	Nitroprusside	Nicardipine	Clevidipine
Hemodynamic Effects	Reduces afterload and preload → <b>may increase ICP</b>	Decreases afterload, minimal effect on preload → improved CPP, CO	Decreases afterload, minimal effect on preload → improved CPP, CO
Onset for hypertension	<b>30-60 secs</b> , peak 2 mins	60 secs, peak 2 mins (w/bolus), $t_{1/2\alpha} = \mathbf{3-15\ min}$	<b>2-4 min</b> , peak 3 min
Distribution & Elimination	Vd = ECF, MetHgb buffer 500 mcg/kg SNP. <b>CN radicals</b> converted to TCN	Vd=7-8 L/kg, 95% highly protein bound. Hepatic metabolism → feces 40%, urine 60%	Poor water solubility → 20% soy-based lipid emulsion 99% protein bound, Vd 0.17 L/kg. <b>Rapid hydrolysis by esterases</b>
Half-life	<b>2-4 minutes</b> (parent); 3 days (thiocyanate)	$t_{1/2\beta} = \mathbf{45\ min}$ $t_{1/2\gamma} = 14.4\ hrs$	$t_{1/2\beta} = \mathbf{1\ min}$ (predominant) $t_{1/2\gamma} = 15\ min$
Titration	Every 5 minutes	Every 5-15 min; decrease dose by 2.5-5 mg/hr once target BP achieved	Double dose every 90 secs; as BP approaches goal, increase dose by less than double every 5-10 mins

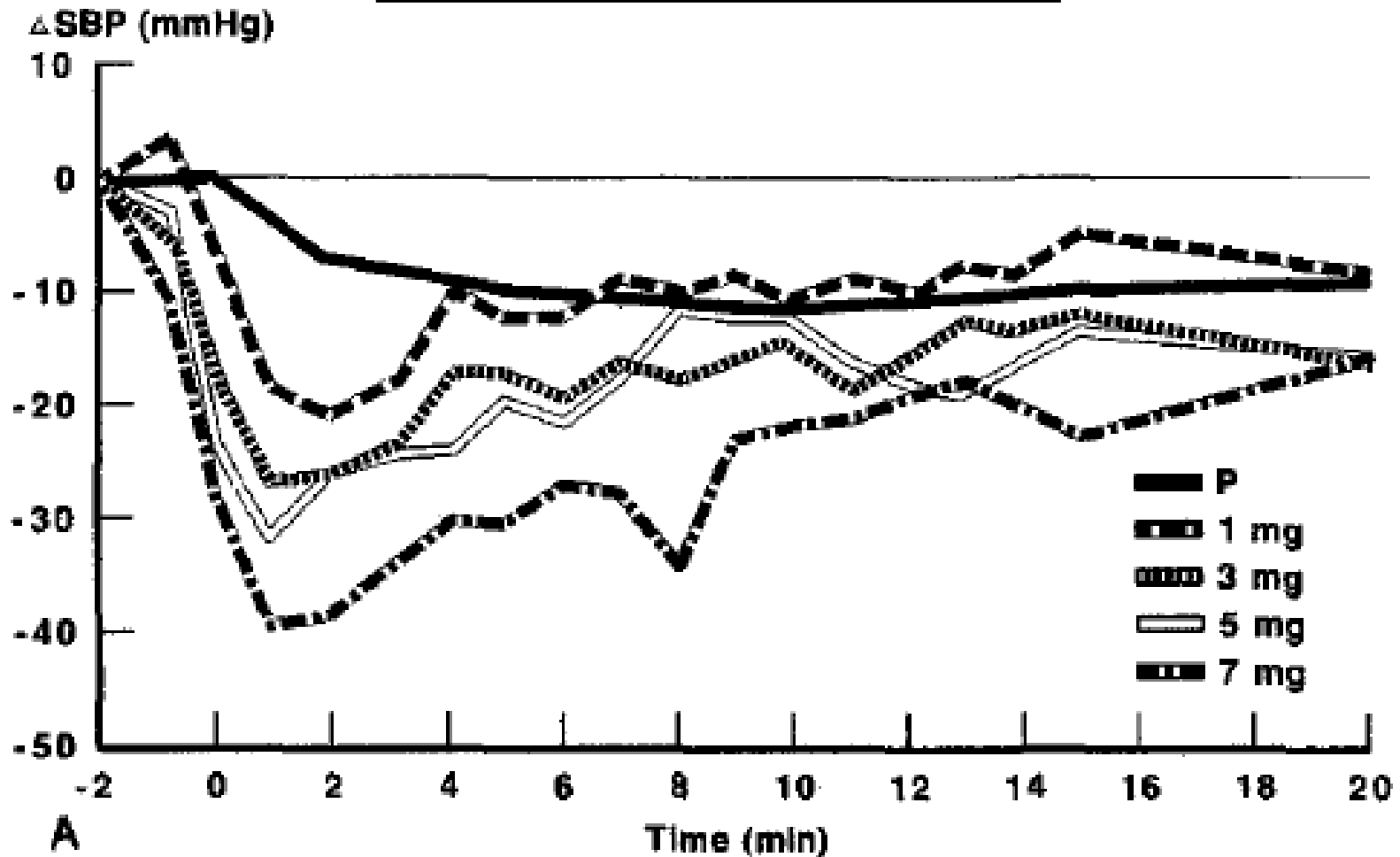
Source: J Anaesth Clin Pharmacol 2014;30:462-71. Circulation 1978;57(4):732-8 Drugs 2006; 66 (13): 1755-1782. Clin Pharmacol Ther 1990;47:706-18. Drugs 2014;74:1947-60

# SNP vs. NIC in Cardiac Surgery

Reference	Patients & Study Design	Intervention & Comparator	Outcomes	Conclusions/ Comment
J Cardio-thorac Vasc Anesth 1991;5(4):357-61.	Open, randomized, multicenter trial  N=74 CABG pts with post-op HTN	<b>NIC 2.5-12.5 mg bolus followed by 2-4 mg/hr infusion</b> , vs. SNP 0.5-6.0 mcg/kg/min	NIC>SNP: goal MAP < 90 mmHg achieved more quickly, ↓ SVR, 2x fewer dose adjustments/24hr SNP>NIC: ↑ HR, 400 mL more blood transfused	<b>Bolus helped NIC achieve BP target faster</b>  NIC is an alternative to SNP
J Cardio-thorac Anesth 1989;3(6):700-6.	Prospective cohort  N=45 CABG pts	<b>NIC 3 mcg/kg/min (≈ 12.5 mg/hr)</b> vs. SNP 1 mcg/kg/min started before surgery	Comparable MAP control ↓ PAP with SNP prior to sternotomy Myocardial ischemia: NIC (9%) vs. SNP (24%) (from induction to start of CPB)	<b>High initial NIC infusion</b> NIC may be a suitable alternative after coronary artery surgery
Am J Cardiol 1989;64(15):22-7H.	Prospective RCT N=120 CABG pts	1:1:1 = <b>NIC 3 mcg/kg/min</b> vs. SNP 1 mcg/kg/min vs. no vasodilator	Comparable MAP control Myocardial ischemia: NIC (10%) vs. SNP (25%) vs. 28% (control)	<b>High NIC infusion rate</b>

# Nicardipine Bolus Pharmacodynamics

## SBP Reductions with Bolus



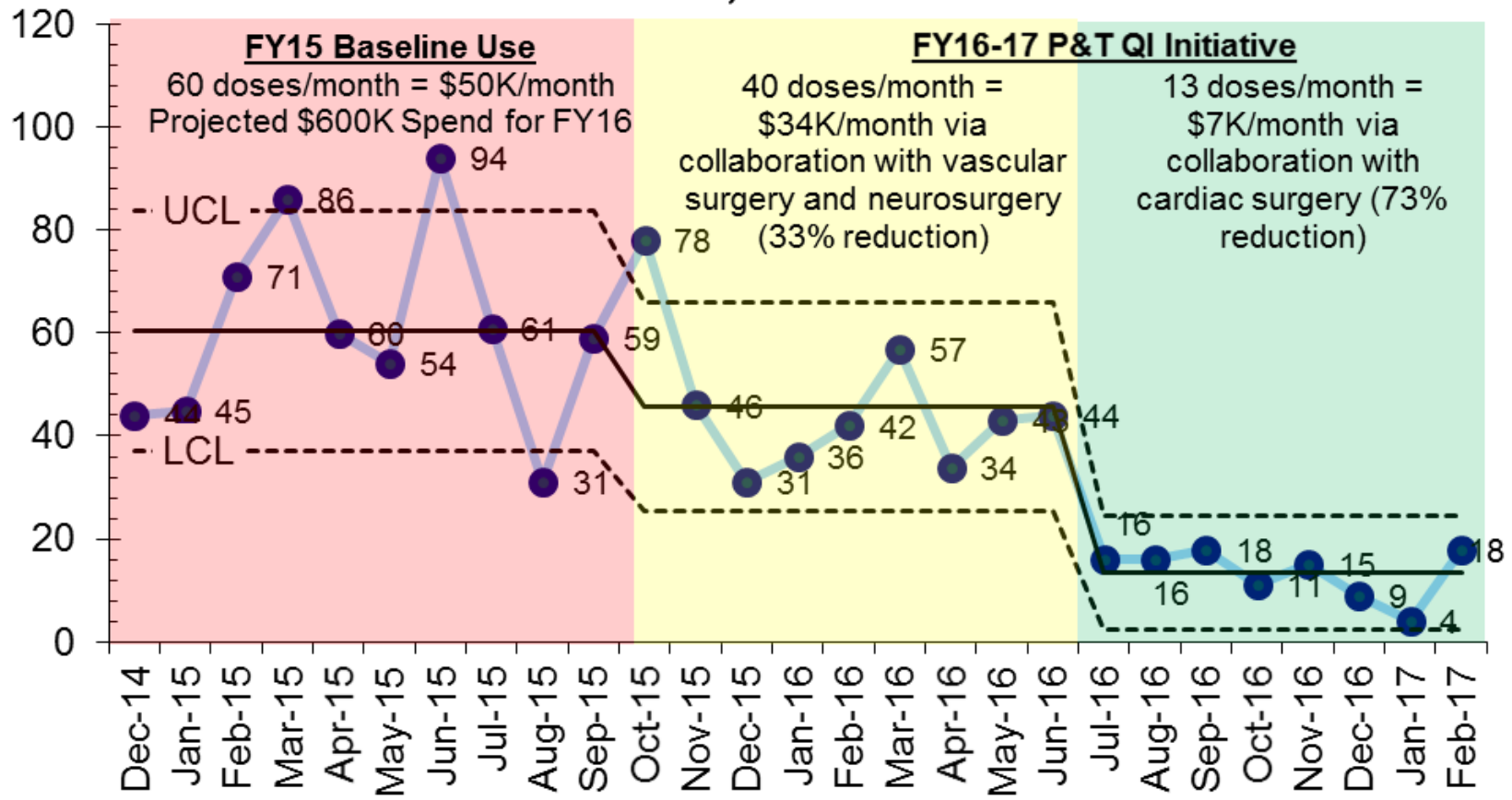


# BMC's Response to SNP Price Hike

- Consider alternatives – revisit clevidipine
- Pharmacy operations modifications
  - Add NIC to ADCs, on override to ICUs
  - Decrease SNP inventory
  - ADC alerts for preparation instructions for nursing, do not give NIC bolus IVP
- Systems improvements
  - Do not automatically dispense SNP from post-op order sets
  - Add NIC bolus from bag, update administration instructions, decrease lower rate limit to 2.5 mg/hr
  - Update smartpumps for ORs and ICUs
- Education about the SNP million dollar sweepstakes

# Outcome Metric – SNP Doses Dispensed (C Chart)

**Count of Monthly Doses Administered of Sodium Nitroprusside  
All Patient Care Areas, December 2014 - Present**



# Lessons Learned- Improvement Science as a Tool



Identify an issue



Collect baseline data



Driver diagram



Define metrics



Track metrics as data over time

# Who Will Be Ready for the Next Price Hike?

## Clinical Pharmacists

- Relationship with prescribers
- Patient, product, process knowledge, and empathy
- Build leadership experience
- Track real-time data (frontline feeling, feedback, observations & patient encounters/med use)
- Demonstrate your value to your team

## Pharmacy Managers

- Administrative and political connections
- Negotiating skills/experience
- Purchasing data and trends and experience
- Ability to negotiate with distributors
- Important scope and perspective (forest, not just trees)

# How We Broke Even

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- Budget
- Strategies
- Outcomes
- Relationships

# Assessment Question #3

Which of the following statements best describe why clinical pharmacists should lead initiatives to combat price hikes?

- A. Knowledge of product, process and patient
- B. Ability to negotiate with distributors
- C. Administrative and political connections
- D. Expertise in analyzing purchasing data

# Response Question #3

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# Summary

- Price hikes and shortages in the ICU are common, relevant, and largely driven by the unapproved drugs initiative
  - Hospital budgets cannot keep up with this inflationary rate
- Improvement science can help demonstrate and sustain success with IV acetaminophen, sodium nitroprusside, and other cost-focused initiatives
- Critical care pharmacists should lead team efforts to mitigate patient and financial harm due to price hikes and shortages



# Special Thanks

- Collaborators

- Nicole Curtis, Paul Huiras, Jennifer Empfield, Jason Mordino, Lindsay Arnold, Kevin Horbowicz, Je Lee and the Willow team

- Champions

- David McAneny, Keith Lewis, Mauricio Gonzalez, Karl Karlson, Alik Farber, Nirav Patel, Jeanette Lee, Courtney Takahashi, Joy Vreeland, David Twitchell

- For more information

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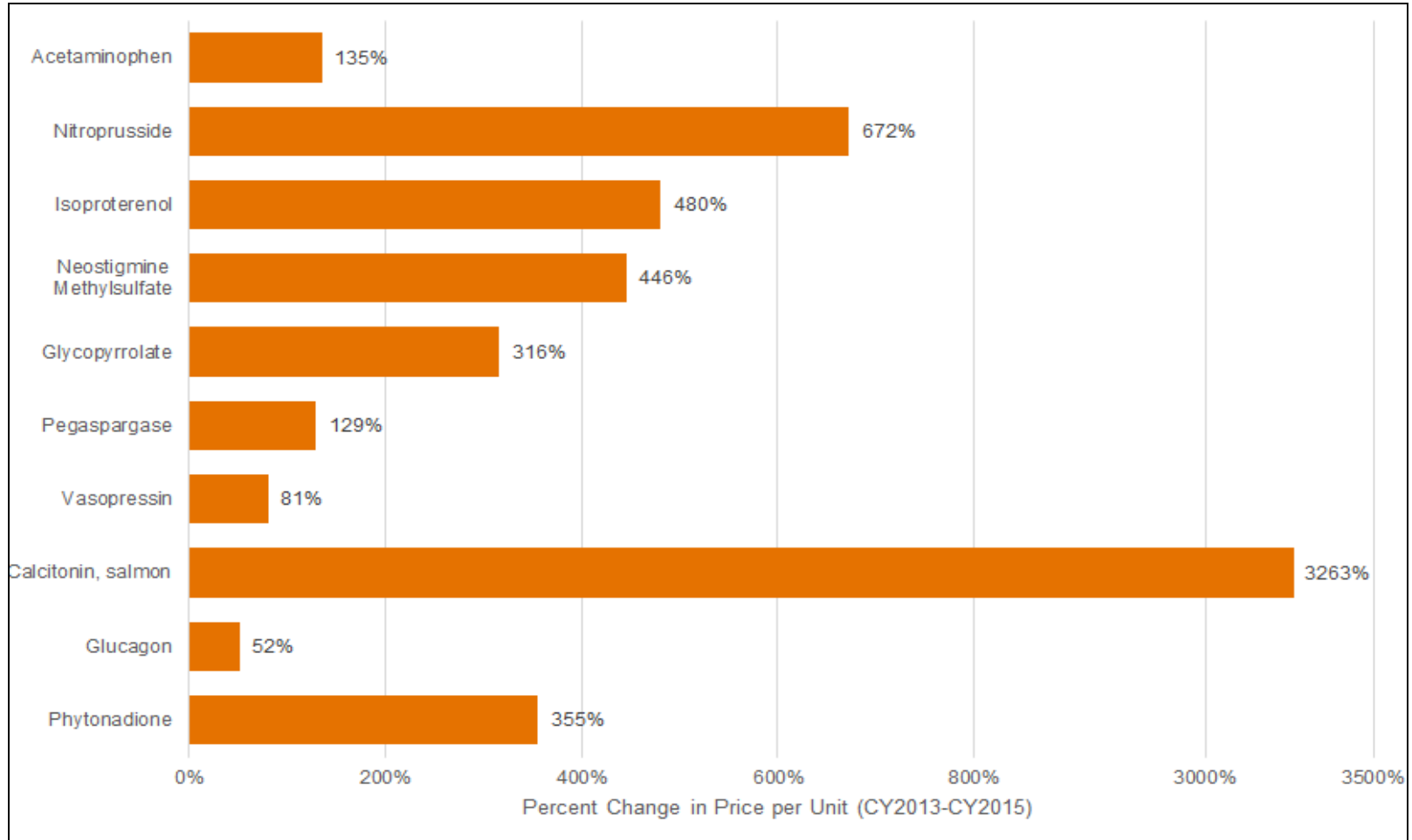


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# Boston Medical Center HEALTH SYSTEM

## Additional Information

# Selected Percent Increases



Trends in hospital inpatient drug costs. National Opinion Research Center. October 11, 2016. Source: [www.aha.org/content/16/aha-fah-rx-report.pdf](http://www.aha.org/content/16/aha-fah-rx-report.pdf)

# \*UDI Ex: Neostigmine

## Top Older Agents with High Growth in 2015

Drug <sup>a</sup>	2015 Expenditures (\$ Thousands)	Percent Change From 2014
Vasopressin	160,977	697.7
Neostigmine	288,273	409.2
Isoproterenol	219,748	275.7
Hydroxyprogesterone	191,250	270.9
Hydroxychloroquine	506,761	237.6
Flucytosine	49,157	126.4
Flecainide	88,321	123.8
Nitroprusside	218,022	112.8

# UDI Ex: Neostigmine

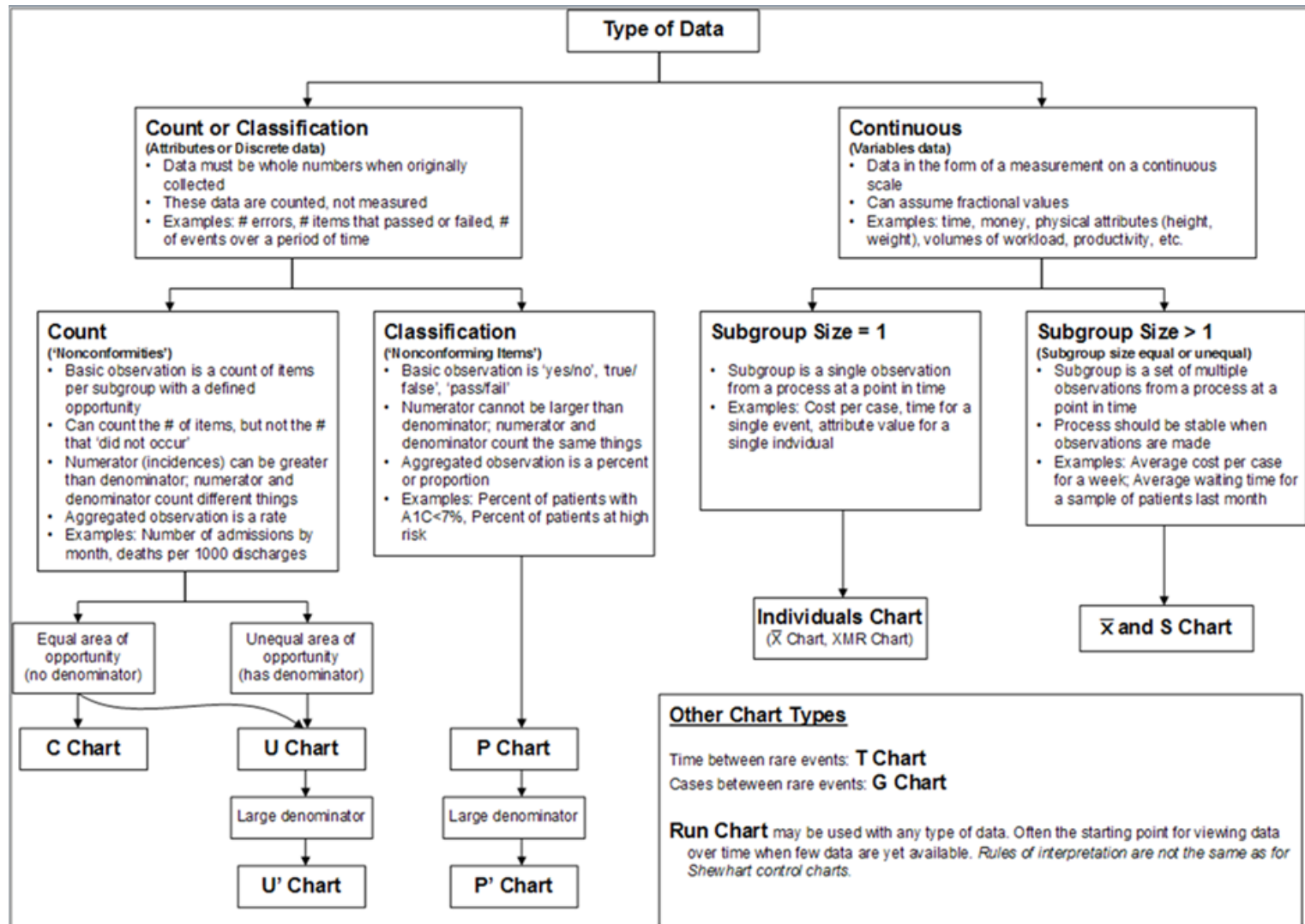
- Received approval for the neuromuscular blockade reversal indication
- Used for decades off label
- Upon approval in 2013
  - Originally this was an Eclat Pharmaceuticals product
  - Manufacturer urged the FDA to disallow all generic competitors of the product
  - Letter claimed that other manufacturers lacked safety data and posed a safety hazard
- Net change from 2014 to 2015: 5%
- National Opinion Research Center Findings:
  - “Drug price increases appear to be random and inconsistent from one year to the next”

# **\*\*Manufacturer Consolidation and Rights**

- Nitroprusside and isoproterenol
  - Originally Hospira products
  - Sold to Marathon (price increase #1)
  - Sold to Valeant (price increase #2)
  
- Neostigmine
  - Eclat sold to Flamel Technologies in 2012
  - Flamel merged with Avadel Pharmaceuticals in 2016
    - Avadel business strategy:
      - Development patent protected products
      - Identification of Unapproved Marketed Drugs
      - Acquisition of commercial/late stage products

Source: Annual Report 10-K. United States Securities and Exchange Commission. Avadel Pharmaceuticals December 31, 2016.

# Statistical Process Control Chart Selection



# Rules for Detecting Nonrandom Change

