No Shortage on Safety: Preventing Safety Issues with Drug Shortages

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Essential to care™

Disclosure

We do not have (nor does any immediate family member have):

- a vested interest in or affiliation with any corporate organization offering financial support or grant monies for this continuing education activity
- any affiliation with an organization whose philosophy could potentially bias my presentation

Objectives

- Recognize how drug shortages can lead to medication safety issues
- Identify potential safety issues given a specific drug shortage strategy
- Create a drug shortage strategy that minimizes the risk for medication errors and adverse events

Drug Shortage & Patient Safety

- Shortages impact multiple steps in medication-use process
- Urgent/emergent with little or no warning
- Can lead to patient harm or death

Patient Safety Impact

- Precise data not available
- Difficult to measure
  - Who did not receive prescribed therapy?
  - Who received substandard alternative?
  - Who experienced harm?
- Most literature describes *potential* impact
- Surveys attempt to quantify
  - Medication errors
  - Adverse drug events
  - Deaths

ISMP. Drug shortages threaten patient safety. July 29, 2010.
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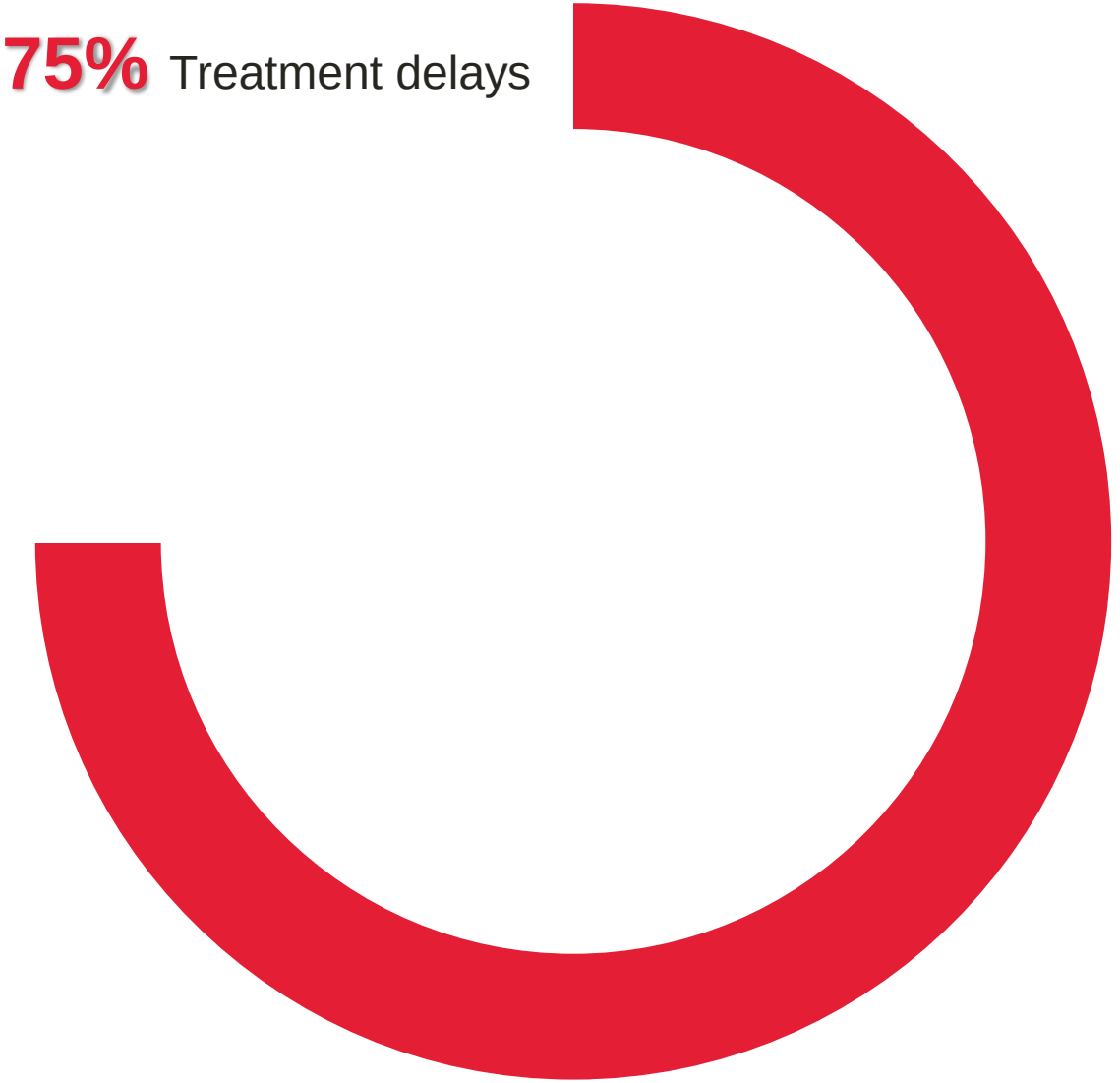
ISMP: Drug shortages continue to compromise patient care. January 11, 2018.

ISMP Survey

Adverse Patient Outcomes

75% Treatment delays



Survey responses:

- Delay in treating sepsis-related acidosis during sodium bicarbonate shortage
- Chemotherapy delays in patient with high chance of remission
- Delay in hypoglycemia treatment when dextrose 50% could not be located in ADC

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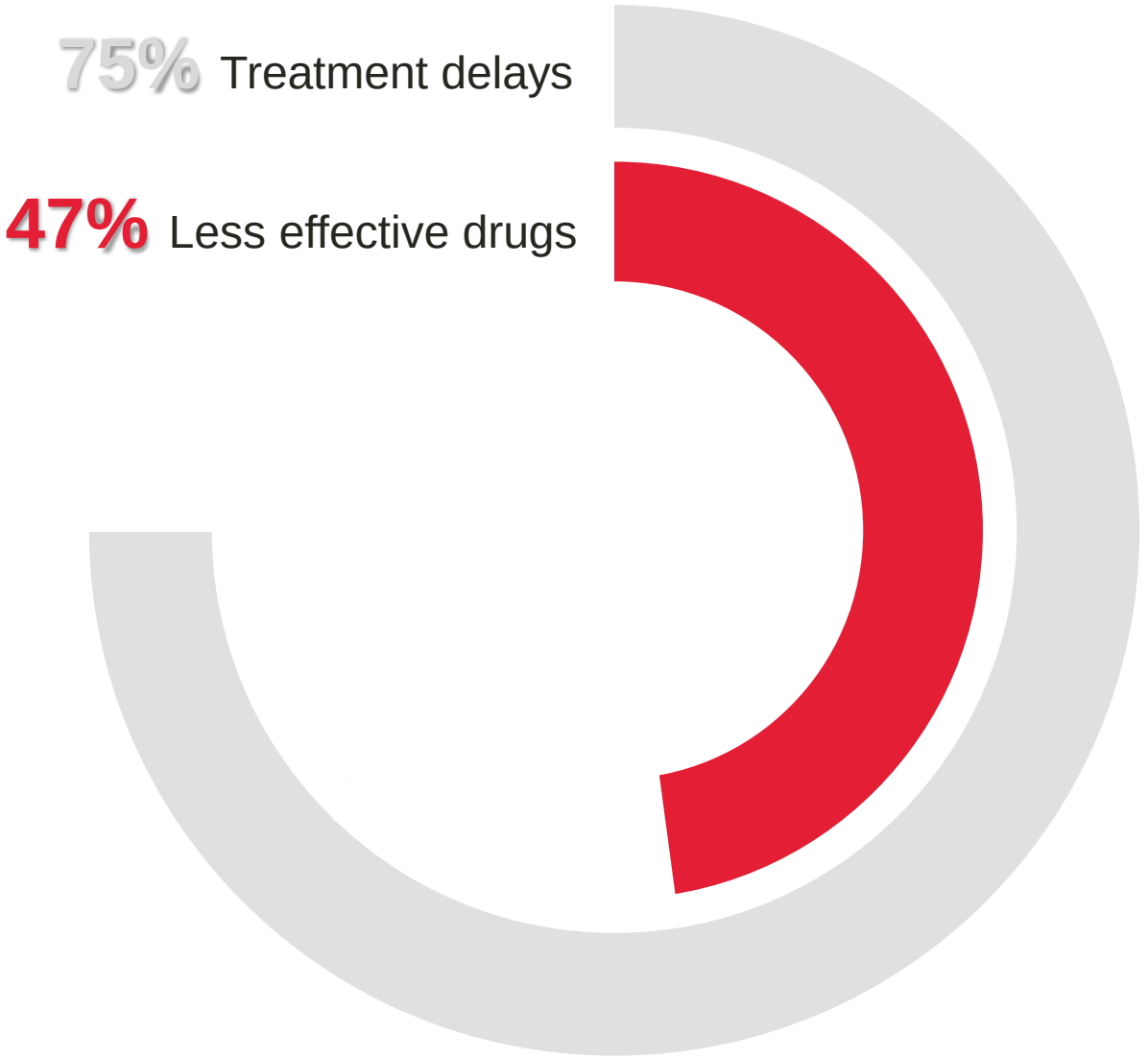
Adverse Patient Outcomes



Survey responses:

- Increased pain during procedure due to inadequate analgesic
- Patient with resistant Pseudomonas infection died when amikacin unavailable
- Inadequate sedation with benzodiazepine led to self-extubation when propofol unavailable

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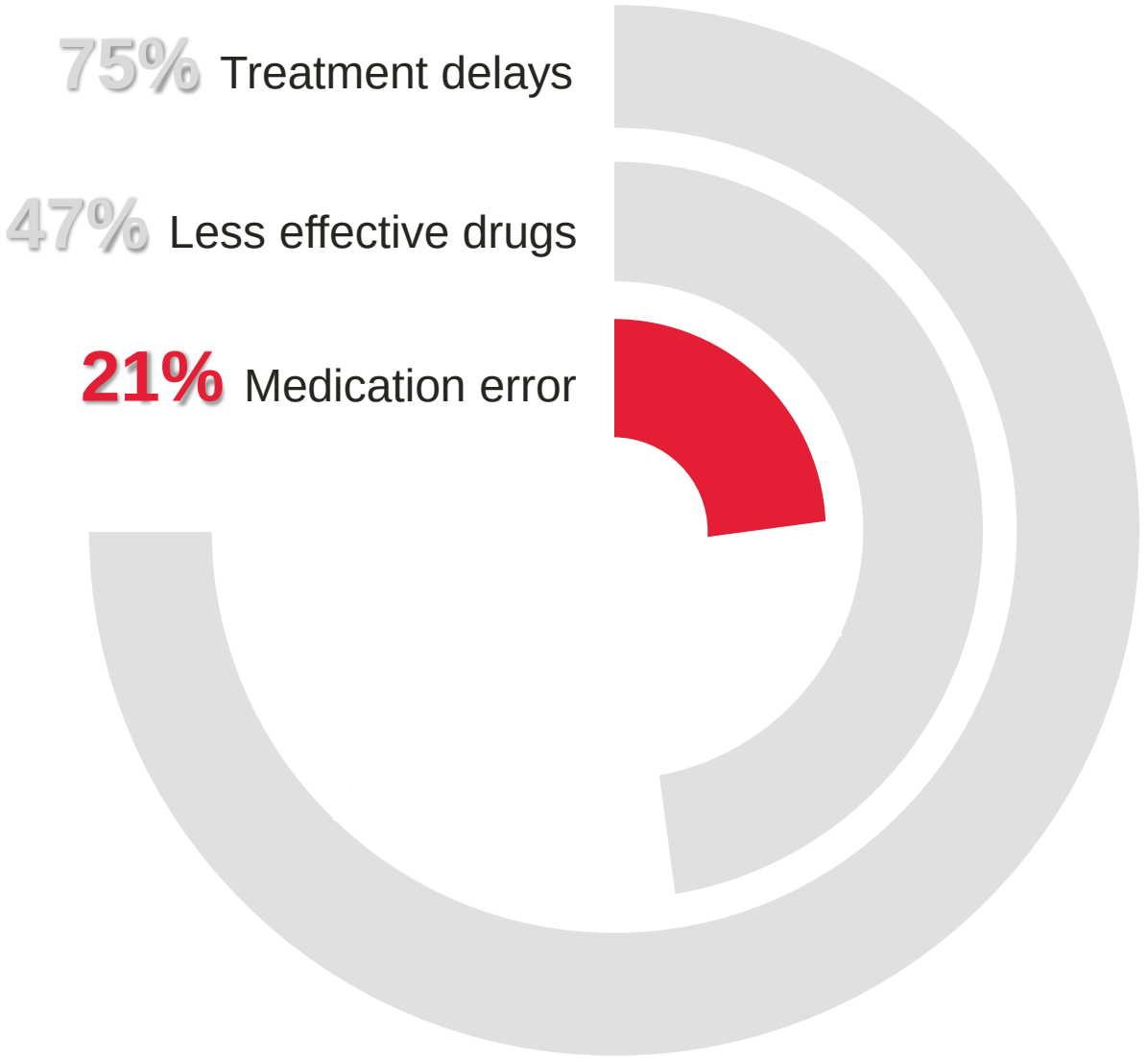
ISMP Survey

Adverse Patient Outcomes

Survey responses:

- Morphine 10 mg/mL vial dispensed & administered when 2 mg/mL vials unavailable
- Epidural made using MDV with preservative when preservative-free unavailable
- Wrong concentration of sodium acetate added to automated compounder, several patients received wrong dose in TPN



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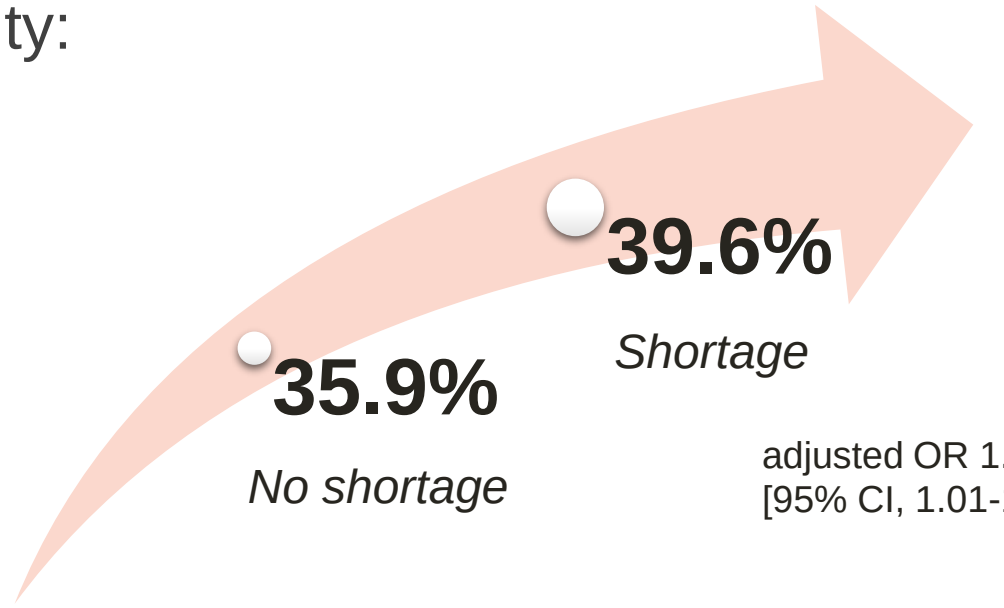
Mortality

Norepinephrine shortage (2011)

- Retrospective cohort of 26 hospitals, 27,835 patients
- Norepinephrine use for septic shock decreased: 77% → 55.7% (↓ ~30%)
- Phenylephrine most frequently used alternative
- In-hospital mortality:



adjusted OR 1.15
[95% CI, 1.01-1.30]; *P*=0.03

Vail E et al. *JAMA* 2017; 317:1433-42.

Drug Shortage & Patient Safety

Same Drug Available

- Packaging
- Strengths
- Manufacturers
- Dosage forms
- Product preparation
- Changes in pharmacy automation
- Look-alike, sound-alike

Alternative Agent or No Alternative

- Efficacy
- Adverse effects
- Dosing
- Drug interactions
- Monitoring
- Treatment delays/rationing
- Look-alike, sound-alike

Alternative Drug Sources

Foreign Supply

- Unknown pedigree
- Less oversight than FDA
- Operational logistics

“Gray” Market

- Cannot be verified or proven safe
- Unknown origin
- Unknown storage
- Cost

Compounding

- 503b must comply with manufacturing standards
- FDA inspection findings & resolutions publicly available

Which shortage situation is likely to lead to the greatest harm?

A. Same drug, different concentration

B. Same drug, but vial instead of prefilled syringe

C. Same drug, different manufacturer/packaging

D. No product available – requires alternative or treatment delay

Answer: It depends!

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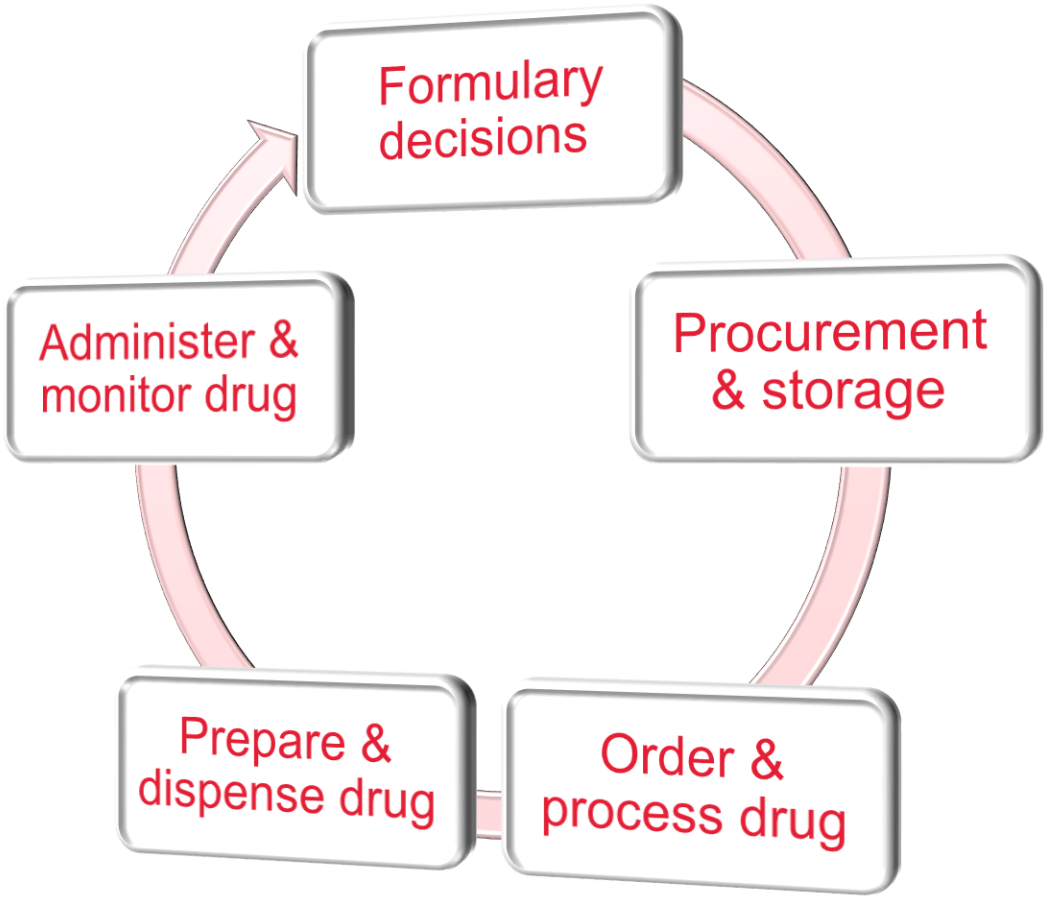
Failure Mode Effects Analysis

Medication Use Process



MacDonald et al. *Hosp Pharm* 2011; 46:943-51.

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Medication Use Process – Vulnerability

Nurse unfamiliar with alternative:

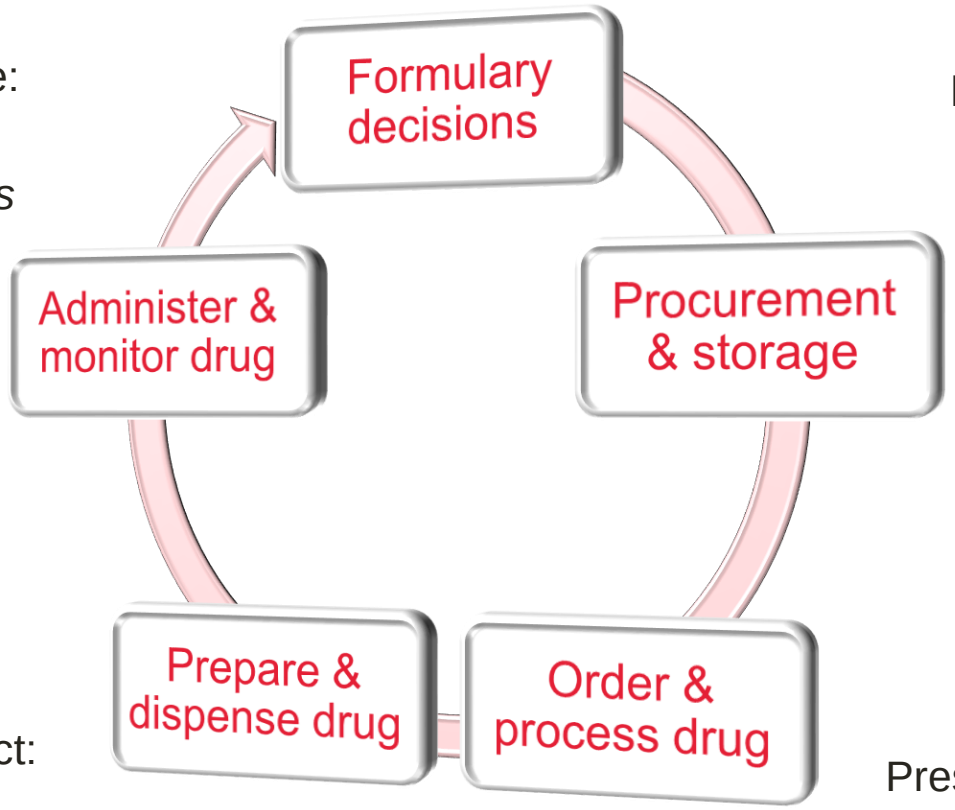
Wrong dose, override safety barriers, miss preventable ADEs

Administer drug using different concentration or route:

Wrong dose, wrong route

Prepare/dispense using different concentration or compounded product:

Wrong dose



Buyer doesn't notify staff:

Sound-alike, look alike

Inventory product into systems:

CPOE, ordersets, ADCs, pharmacy storage, barcode systems

Prescriber unaware of shortage:

Delays treatment

Prescriber unfamiliar with alternative:

Orders wrong dose

Pharmacist unfamiliar with alternative:

Verifies wrong dose or misses interaction

MacDonald et al. *Hosp Pharm* 2011; 46:943-51.

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Which shortage situation is likely to lead to the greatest harm?

	FMEA themes:
A. Same drug, different concentration	***Wrong dose***
B. Same drug, but vial instead of prefilled syringe	***Look-alike, sound-alike***
C. Same drug, different manufacturer/packaging	***Look-alike, sound-alike***
D. No product available – requires alternative or treatment delay	***Unfamiliarity, wrong dose/route, less effective alternative, delays***

MacDonald et al. *Hosp Pharm* 2011; 46:943-51.

Shortage Scenario #1

Worldwide pandemic has led to shortage of fentanyl injection

Details

- Biggest use is ICU analgesia
- Normally compound drips using 2500 mcg/5 mL vials
- Currently only able to get 250 mcg/5 mL vials
- Causing secondary shortages of other injectable opioids

Strategy

- Restrict to ICU – drips only
- Hydromorphone or morphine injection for intermittent/PRN
- Use 10 x 250 mcg/5 mL vials to make drips
- If no fentanyl, use hydromorphone or morphine as infusion also
- Consider fentanyl patches

Can you spot the vulnerabilities?

Shortage Scenario #1

Strategy		Potential Vulnerability
Restrict to ICU – drips only	→	• Patients outside ICU receiving less effective analgesia? • Embedded in order sets or prescriber unaware – delays treatment
Hydromorphone & morphine as alternatives	→	• Are providers as familiar with dosing, monitoring, ADRs? • Are these in order sets or ordered “freehand”? Verbal orders? • Are these built in smart pump libraries? • Are patients receiving safe and effective analgesia? Allergies? Renal failure? Delirium?
Using 10 x 250 mcg/5 mL vials to compound drips	→	• Errors using different products/concentrations • Treatment delays
Fentanyl patches	→	• Absorption issues – less effective?
Storage	→	• Are alternatives readily available/stored on unit?

Shortage Scenario #2

"Manufacturing delay" has led to a shortage of epinephrine pre-filled syringes

Details

- Stocked in all code carts and ADCs throughout hospital
- Various vials sizes/strengths remain available
- FDA has allowed for extended BUD for some lots of syringes

Strategy

- Remove from ADCs
- Reduce par in code carts from 5 to 2
- Replace other 3 syringes with 1 mg/mL ampule in "kit" with filter needle, 0.9% NaCl, and syringe
- Pharmacists responding to codes may carry 30 mg/30 mL MDV to draw up 1 mg doses

Can you spot the vulnerabilities?

Shortage Scenario #2

Strategy		Potential Vulnerability
Remove from ADCs	→	• Treatment delay – needed emergently • Replaced with vials?
Reduce par in code carts, replace with vial “kit”	→	• Lack of standardization • Unfamiliarity with “kit” components/process • Potential to fill with wrong concentration
Pharmacists using MDV	→	• Potential to administer wrong dose • 24/7 pharmacist response?
Extended BUD	→	• FDA doesn’t recommend re-labeling • Tracking
Storage	→	• Look-alike, sound-alike • ePHEDrine has been dispensed instead of EPINEPHrine

Shortage Scenario #3

Shortage of injectable loop diuretics due to "unknown reasons"

Details

- Furosemide most prescribed
- Furosemide in ICU and cardiac floor ADCs
- Bumetanide alternative
- Intermittent supply of both
- Ethacrynic acid use restricted due to high cost

Strategy

- Remove furosemide from ADCs
- Encourage IV to PO (including torsemide PO)
- Interchange furosemide & bumetanide IV based on availability per P&T policy
- Equipotent dosing chart developed to assist with interchanges

Can you spot the vulnerabilities?

Shortage Scenario #3

Strategy	Potential Vulnerability
Remove from ADCs	• Treatment delay • Acute pulmonary edema – could avoid intubation
Encourage IV to PO (including torsemide)	• Switching between IV-PO and different drugs • Dosing errors • Absorption issues with PO
Intermittent supply of both	• Different manufacturers, packaging, concentrations • Which one do we have today? – treatment delay
Interchange based on availability	• Dosing errors • Nurse looking for wrong drug – treatment delay • Sent home with different drug than home med
Ethacrynic acid as last resort	• Less familiar with dosing & administration can lead to errors • Adverse effects

Checklist

Determine the Impact the Shortage Will Have

- Operational / Information Technology (IT)
  - How long it will affect you
  - How long you can last
  - Response system in place
  - What needs to change with all IT systems
- Clinical / Therapeutic
  - Similar agents on formulary / in the market (all available options)
  - Patients most affected
  - Side effect profile / safety comparisons and safety considerations
- Financial
  - Calculate the cost impact

Response System

- Always have a system in place
  - Assign responsibility
  - Outline process
  - Involve all practitioners / stakeholders
    - Pharmacy staff, nursing, physicians, IT, education, administration
  - Be quick to respond
  - Break down IT barriers
    - Safety mandates this

Actions to Consider When Replacing a Product

- Remove all remaining current product simultaneously
- Ensure new product is only one available for order entry / pumps
- Change all patient drug orders to match new product
- Replace inventory completely – in pharmacy, other storage and automated dispensing cabinets
  - Ensure other product is not used
  - Verify barcode, test clinical decision support alerts

More Actions to Consider…

- Communicate, communicate, communicate
- Implement forcing functions within IT systems
- Ensure vital information / directions also included on medication administration record
- Ensure availability of correct syringes, equipment for administration
- High risk

Words of Wisdom

Borrow from your policies / procedures / guidelines for adding new agents to formulary or nonformulary considerations.

Make it easy to do the right thing and impossible to do the wrong thing.

Plan for human fallibility.

Look for the Silver Lining – and unexpected sources

- Was the drug being used appropriately before it became unavailable?

and unexpected sources

efore it became unavailable?

Drug Shortage Management Checklist

PHARMACY PRACTICE NEWS

FEBRUARY 15, 2018

Checklist Designed to Help Manage Drug Shortages

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Cardinal Health

https://www.pharmacypracticenews.com/Policy/Article/03-18/Checklist-Designed-to-Help-Manage-Drug-Shortages/46988

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Sample page

Status	Action Item	Responsible Person(s)	Comments/ Progress
Operational/IT Considerations			
	Leader/owner assigned to this shortage (responsible for assigning all tasks/duties and ensuring all are completed)		
	Expected duration of shortage (as reported by manufacturer, ASHP, FDA, other reliable source); update as information becomes available		
	Determine total units remaining on-site (pharmacy stock, remote stock, automation, carts, boxes, trays, clinics, etc.), and off-site, such as in surgery and diagnostic centers		
	Calculate days' supply remaining based on purchase history and utilization		
	Retrieve all units and return to central pharmacy storage for discretionary dispensing (decision based on calculated days' supply available and feasibility)		
	Run report of all patients who currently have orders for the unavailable agent		
	If unavailable agent is included in smart pump library, suppress/delete it and enter the new agent (ensure this is done simultaneously with the changing of the IV bag currently connected to the pump)		
	Ensure all pumps have been updated to reflect most recent library and changes related to this shortage		
	Set up process with IT to prioritize addition of new agent to charge description master, smart pump libraries and related systems		
	Ensure availability of correct syringes, equipment for administration of new agent (work with materials services to procure and change stock)		
	If it is determined that the best action is to use formulary agent in place of unavailable agent, then (not necessarily in this order): • verify availability of new agent (in-house and wholesaler/?manufacturer) • order new product as needed (based on use)		

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- Nicol N. “Checklist Designed to Help Manage Drug Shortages.” *Pharmacy Practice News*. March 14, 2018, https://www.pharmacypracticenews.com/Policy/Article/03-18/Checklist-Designed-to-Help-Manage-Drug-Shortages/46988. Accessed September 18, 2020.

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