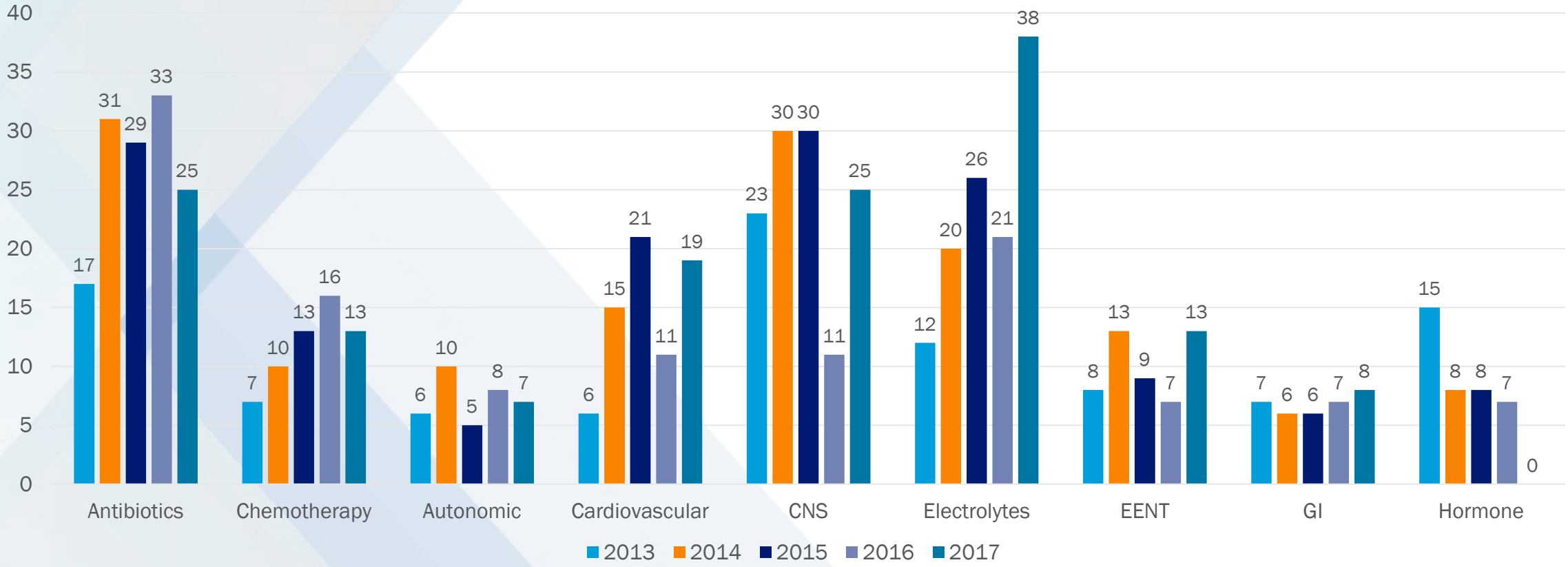
Baxter

CRRT in the Era of Drug Shortages

Continuous Renal Replacement Therapy in the Era of Drug Shortages



Drug Shortages Are the New Normal

2012

BUSINESS DAY

Drug Shortages Persist in U.S., Harming Care

By KATIE THOMAS NOV. 16, 2012

http://www.nytimes.com/2012/11/17/business/drug-shortages-are-becoming-persistent-in-us.html Accessed 2/9/2018

2016

https://www.nytimes.com/2016/01/29/us/drug-shortages-forcing-hard-decisions-on-rationing-treatments.html Accessed 2/9/2018

2014

HEALTH

Drug Shortages Continue to Vex Doctors

By SABRINA TAVERNISE FEB. 10, 2014

https://www.nytimes.com/2014/02/11/health/shortages-of-critical-drugs-continue-to-vex-doctors-study-finds.html Accessed 2/9/2018

2017

HEALTH

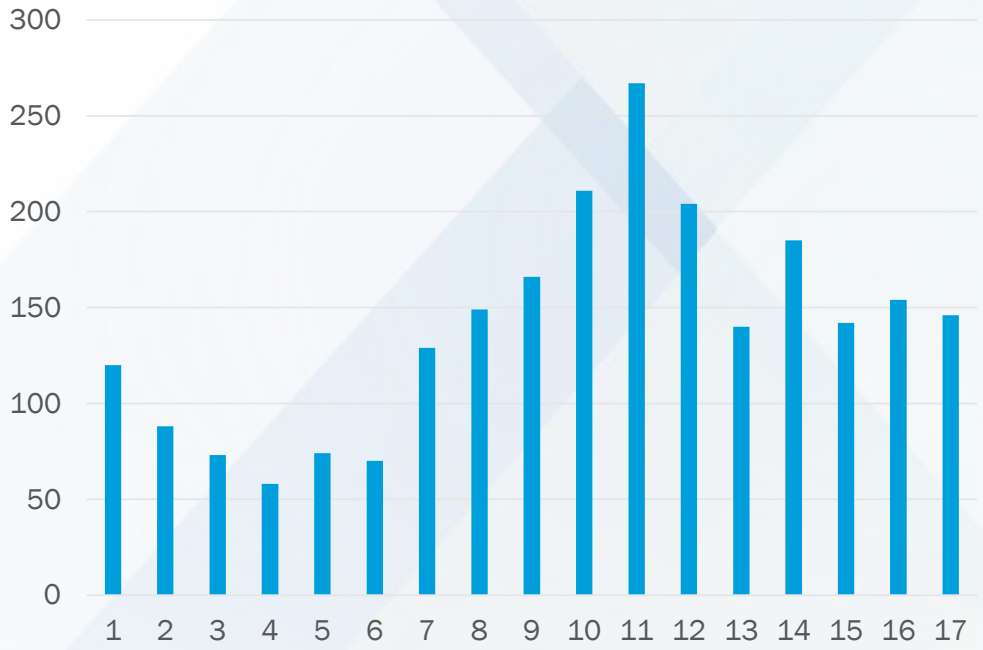
U.S. Hospitals Wrestle With Shortages of Supplies Made in Puerto Rico

By KATIE THOMAS OCT. 23, 2017

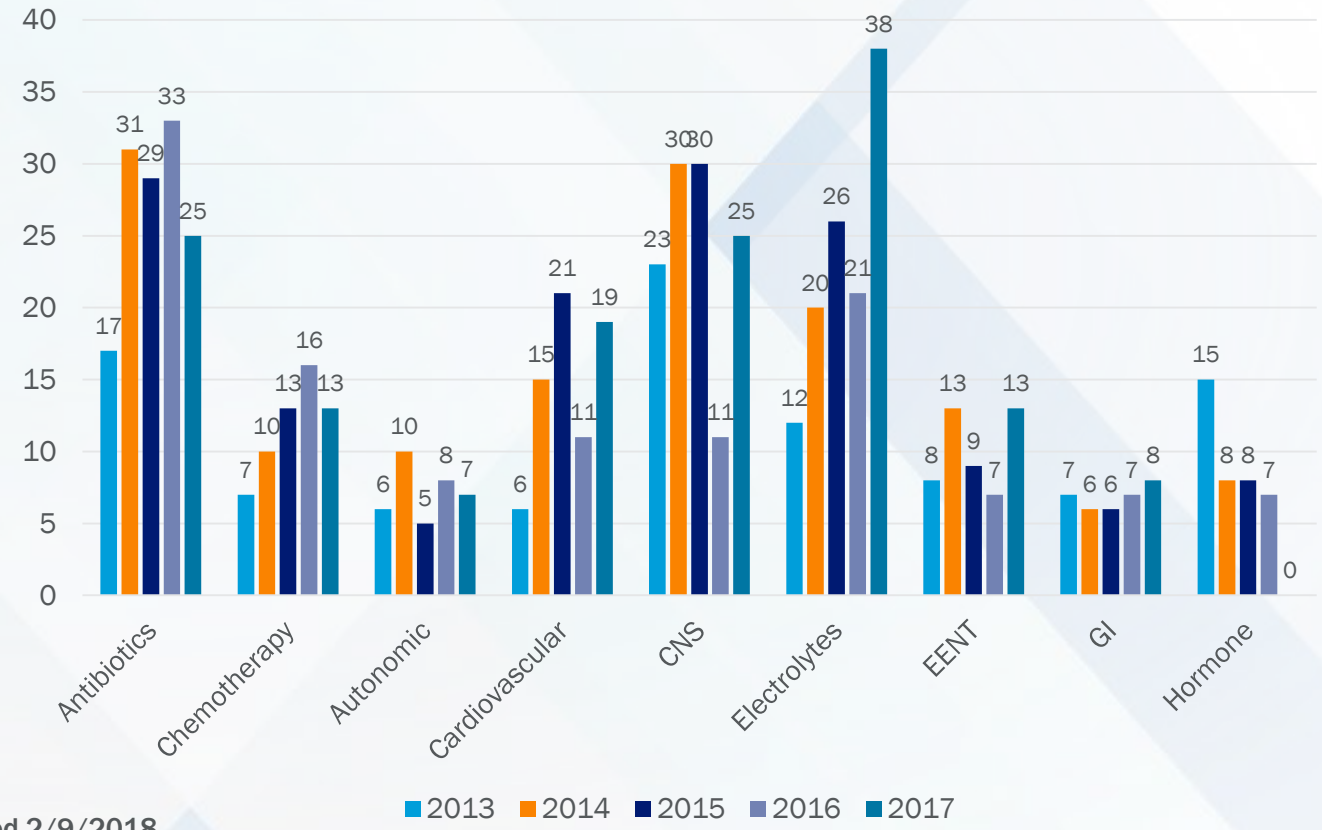
https://www.nytimes.com/2017/10/23/health/puerto-rico-hurricane-maria-drug-shortage.html Accessed 2/9/2018.

Shortages of Key Medicines Represent An Ongoing Challenge

National Drug Shortages: Annual New Shortages by Year
January 2001 to December 31, 2017



National Drug Shortages: Common Drug Classes in Short Supply
New Shortages Reported: 2013–2017



https://www.ashp.org/Drug-Shortages/Shortage-Resources/Drug-Shortages-Statistics Accessed 2/9/2018

Critical Care Providers Must Manage Shortages on a Daily Basis

The impact of shortages is amplified in critical care settings

- Required care is high-intensity and time-sensitive
- Shortages disproportionately impact sterile injectable medications commonly used in critical care settings
- Alternative medications may not be available
- When available, alternative medications may increase the likelihood of medication errors (due to unfamiliarity) or toxicity (due to less favorable profiles compared to first-line agents)
- Treatment delays can adversely affect patient outcomes

Mazer-Amirshahi et al. J Crit Care. 2017 Oct;41:283-288.

Critical Care Drug Landscape (2001-2016)

Contents lists available at ScienceDirect

Journal of Critical Care

journal homepage: www.jccjournal.org

ELSEVIER

U.S. drug shortages for medications used in adult critical care (2001–2016)☆

Maryann Mazer-Amirshahi [a,b,*], Munish Goyal [a,b], Suleman A. Umar [c], Erin R. Fox [d], Mark Zocchi [e], Kristy L. Hawley [f], Jesse M. Pines [e,g]

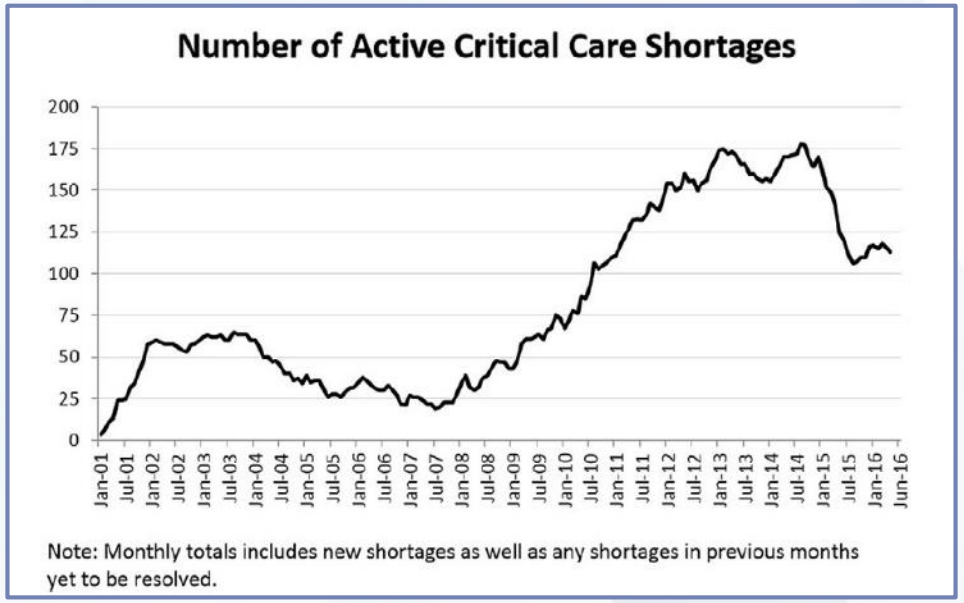
[a] Department of Emergency Medicine, MedStar Washington Hospital Center, 110 Irving Street NW, Washington, DC 20010, United States
[b] Georgetown University School of Medicine, 3900 Reservoir Road, Washington, DC 20007, United States
[c] Department of Internal Medicine, MedStar Washington Hospital Center, 110 Irving Street NW, Washington, DC 20010, United States
[d] Department of Pharmacy and Drug Information Services, University of Utah, 50 N. Medical Drive A050, Salt Lake City, UT 84132, United States
[e] Center for Healthcare Innovation and Policy Research, the George Washington University, 2300 Eye Street NW, Washington, DC 2007, United States
[f] Department of Surgery, MedStar Union Memorial Hospital, 201 E. University Parkway, Baltimore, MD 21218, United States
[g] Department of Emergency Medicine, the George Washington University, 900 23rd Street NW, Washington, DC 20007, United States

ARTICLE INFO

Keywords:
Critical care
Drug shortages

ABSTRACT

Purpose: We describe trends in U.S. shortages impacting critical care drugs from 2001 to 2016.
Materials and methods: Shortages within the scope of critical care were identified using data from the University of Utah Drug Information Services. Shortage characteristics were described using standard descriptive statistics and regression analysis.



Retrospective analysis of data from the University of Utah Drug Information Service

- 24.6% of shortages were for drugs used in high acuity or life-threatening conditions
- No alternative was available for 11.7%, while 24.9% of available alternatives were also impacted by shortage
- The therapeutic category “fluids, electrolytes, nutrition” experienced 7 shortages, lasting a median duration of 8 months

Mazer-Amirshahi et al. J Crit Care. 2017 Oct;41:283-288.

The Sodium Bicarbonate Shortage: A “Basic” Example

How a baking soda shortage became a health-care crisis

Nathan Bomey, USA TODAY Published 3:57 p.m. ET May 31, 2017

(Photo: DON EMMERT, AFP/Getty Images)

CONNECT TWEET 48 LINKEDIN 3 COMMENT EMAIL MORE

A breakdown in the supply chain of sodium bicarbonate — the same basic compound as household baking soda — for use in medical procedures is expected to limit access to certain treatments in hospitals through the end of the year.

A shortage of the antacid is prompting health care providers to carefully prioritize procedures, delay some operations and choose alternative treatments in some instances.

The crisis is directly connected to troubles at a supplier of pharmaceuticals giant Pfizer, but it has rippled through the medical sector, which relies on it to treat various

A Vital Drug Runs Low, Though Its Base Ingredient Is in Many Kitchens

By KATIE THOMAS MAY 21, 2017

RELATED COVERAGE


Drug Shortages Forcing Hard Rationing Treatments JAN. 29, 2


Drug Shortages Continue to V FEB. 10, 2014

Drug Shortages Are Becoming Persistent NOV. 16, 2012

Drug Makers Stalled in a Cycl Lapses and Shortages OCT. 17, 2

Society of Critical Care Medicine
The Intensive Care Professionals

SCCM > Communications > Critical Connections > Archives > A "Basic" Reality: Managing Sodium Bicarbonate and Acetate Shortages

A “Basic” Reality: Managing Sodium Bicarbonate and Acetate Shortages

2017 - 6 December – Giving and Volunteerism

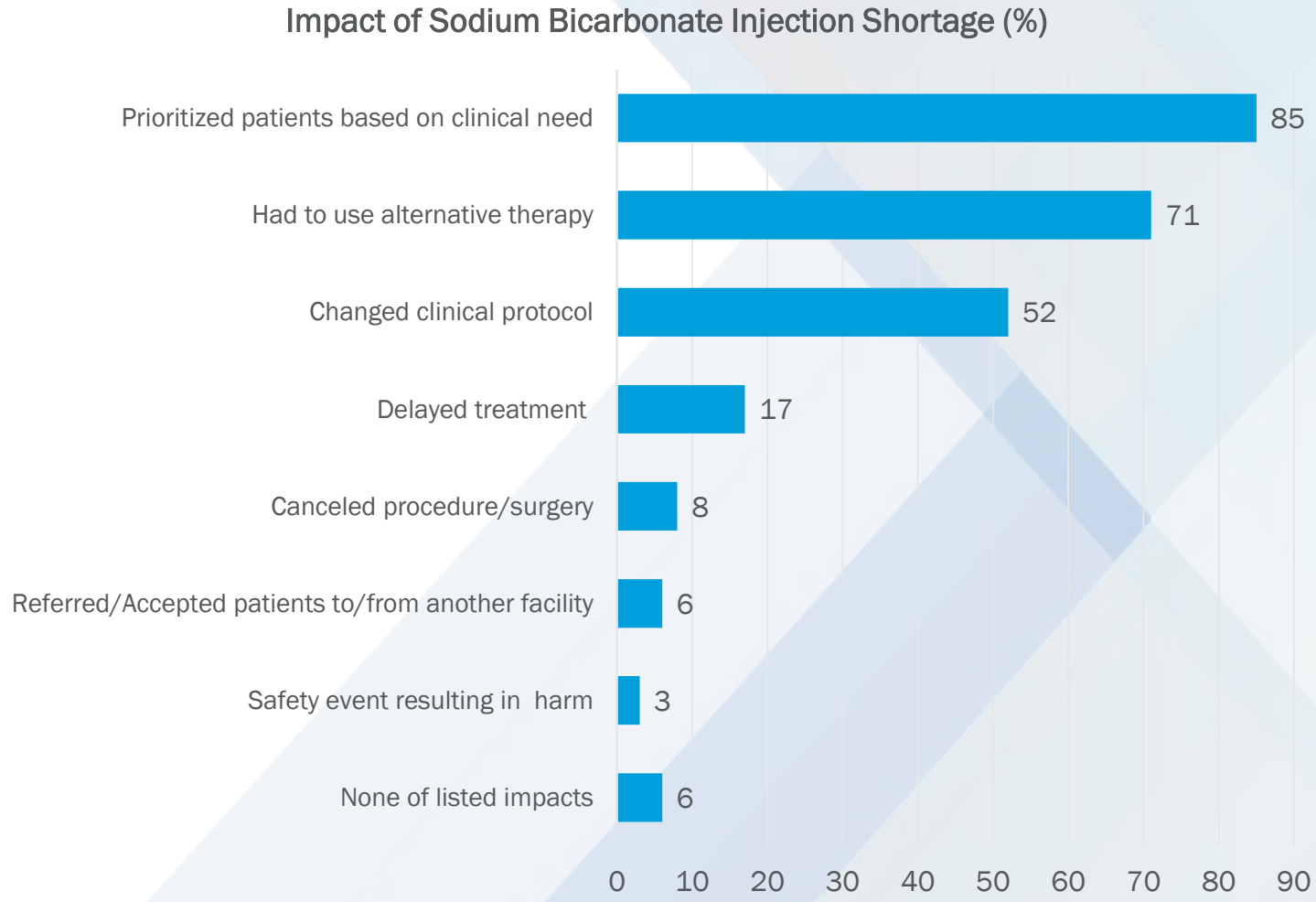
Earnest Alexander, Jr, PharmD, BCCCP, FCCM; Ahmed A. Mahmoud, PharmD, BCCCP; April Miller Quidley, BCCCP, BCPS, PharmD

https://www.usatoday.com/story/money/2017/05/31/how-baking-soda-shortage-became-health-care-crisis/102320494/ Accessed 2/5/201
https://www.nytimes.com/2017/05/21/health/sodium-bicarbonate-solution-critical-shortage-hospitals.html Accessed 2/5/2018
http://www.sccm.org/Communications/Critical-Connections/Archives/Pages/Managing-Sodium-Bicarbonate-and-Acetate-Shortages.aspx Accessed 2/5/2018

The Sodium Bicarbonate Shortage Affects Hospitals' Daily Operations

ASHP Center on Medication Safety and Quality Survey

- 62% of respondents rated the shortage as severe and impacting their hospitals' daily operations and patient care
- 85% of respondents reported needing to prioritize patients' access to sodium bicarbonate injection on the basis of clinical need



Thompson CA. Am J Health Syst Pharm. 2017 Aug 15;74(16):1208-1210.

Compounded IV Products are Associated with More Medication Errors

- Observational study of intravenous product compounding at five U.S. hospitals
- Ready-to-use products were evaluated in two of the study hospitals
- The mean error rate for compounded IV mixtures was 9% (145 errors, 1679 doses) vs. 0.3% (2 errors, 746 doses) for ready-to-use products
- The most common compounding error was deviation from the labeled dose (69%), followed by incorrect base solution volume/content (16%)

"The clear difference in error rates between ready-to use products…and compounded admixtures…suggests that limiting the number of manipulations that must be performed to prepare a product reduces the likelihood of errors"

Table 3.
Error Rates for Compounding I.V. Admixtures

Hospital	Total No. Errors Observed	Total No. Doses Observed	Mean ± S.D. Daily Error Rate (%)
Mountain	27	417	6 ± 3
Midwest	38	440	9 ± 9
Pacific	24	265	9 ± 8
Southeast	31	313	10 ± 5
Northeast	25	244	10 ± 3
Total	145	1679	9 ± 6

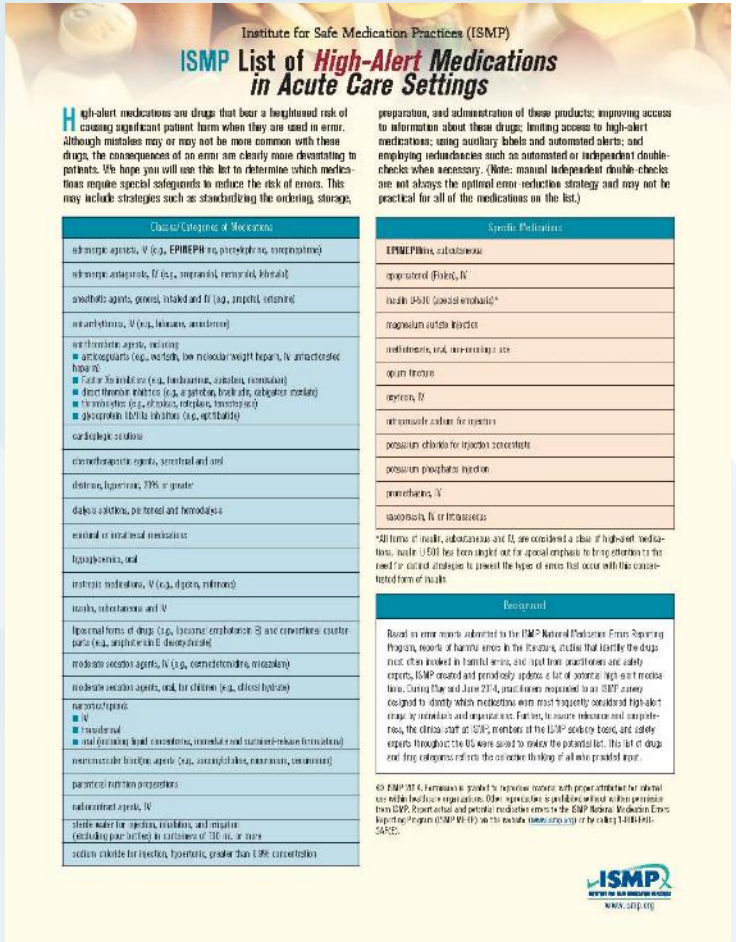
Table 4.
Types of Errors Observed in I.V. Admixtures

Error Category	No. Errors					Total No. Errors (%)
	Mountain	Midwest	Pacific	Southeast	Northeast	
Unauthorized drug	9	0	1	0	0	10 (7)
Wrong dose (as % deviation from labeled dose)						
5.0–9.9	7	11	9	10	10	47 (32)
10.0–14.9[a]	0	6	4	9	2	21 (15)
≥15.0[b]	1	9	5	6	11	32 (22)
Wrong base solution						
Volume	1	1	1	5	0	8 (6)
Content	8	5	0	0	2	15 (10)
Omission	1	0	4	0	0	5 (3)
Wrong preparation technique	0	6	0	1	0	7 (5)

[a]For example, fluorouracil (11% deviation from labeled dose), potassium chloride (10%), and tobramycin (10%).
[b]For example, leucovorin (100% deviation from labeled dose), insulin (60%), dopamine (20%), and ciprofloxacin (33%).

Flynn et al. Am J Health Syst Pharm 1997 May 1;54(9):1110.

Dialysis Solutions Are "High-Alert" Medications That Benefit from Standardization



Institute for Safe Medication Practices (ISMP)

ISMP List of *High-Alert* Medications in Acute Care Settings

High-alert medications are drugs that bear a heightened risk of causing significant patient harm when they are used in error. Although mistakes may or may not be more common with these drugs, the consequences of an error are clearly more devastating to patients. We hope you will use this list to determine which medications require special safeguards to reduce the risk of errors. This may include strategies such as standardizing the ordering, storage, preparation, and administration of these products; improving access to information about these drugs; limiting access to high-alert medications; using auxiliary labels and automated alerts; and employing redundancies such as automated or independent double-checks when necessary. (Note: manual independent double-checks are not always the optimal error-reduction strategy and may not be practical for all of the medications on the list.)

Class/Categories of Medications	Specific Medications
adrenergic agents, IV (e.g., **EPINEPH**rine, phenylephrine, norepinephrine)	**EPINEPH**rine, subcutaneous
adrenergic antagonists, IV (e.g., propranolol, metoprolol, labetalol)	esmolol (Brevibloc), IV
anesthetic agents, general, inhaled and IV (e.g., propofol, ketamine)	insulin U-500 (concentrated)*
antiarrhythmics, IV (e.g., lidocaine, amiodarone)	magnesium sulfate injection
antithrombotic agents, including ■ anticoagulants (e.g., warfarin, low molecular weight heparin, IV unfractionated heparin) ■ Factor Xa inhibitors (e.g., fondaparinux, apixaban, rivaroxaban) ■ direct thrombin inhibitors (e.g., argatroban, bivalirudin, dabigatran etexilate) ■ thrombolytics (e.g., alteplase, reteplase, tenecteplase) ■ glycoprotein IIb/IIIa inhibitors (e.g., eptifibatide)	methotrexate, oral, non-oncology use
cardioplegic solutions	opium tincture
chemotherapeutic agents, parenteral and oral	oxytocin, IV
dextrose, hypertonic, 20% or greater	nitroprusside sodium for injection
dialysis solutions, peritoneal and hemodialysis	potassium chloride for injection concentrate
epidural or intrathecal medications	potassium phosphates injection
hypoglycemics, oral	promethazine, IV
inotropic medications, IV (e.g., digoxin, milrinone)	vasopressin, IV or intraosseous
insulin, subcutaneous and IV	
liposomal forms of drugs (e.g., liposomal amphotericin B) and conventional counterparts (e.g., amphotericin B deoxycholate)	
moderate sedation agents, IV (e.g., dexmedetomidine, midazolam)	
moderate sedation agents, oral, for children (e.g., chloral hydrate)	
narcotics/opioids ■ IV ■ transdermal ■ oral (including liquid concentrations, immediate and sustained-release formulations)	
neuromuscular blocking agents (e.g., succinylcholine, rocuronium, vecuronium)	
parenteral nutrition preparations	
radiocontrast agents, IV	
sterile water for injection, inhalation, and irrigation (excluding pour bottles) in containers of 100 mL or more	
sodium chloride for injection, hypertonic, greater than 0.9% concentration	

Background

Based on error reports submitted to the ISMP National Medication Errors Reporting Program, reports of harmful errors in the literature, studies that identify the drugs most often involved in harmful errors, and input from practitioners and safety experts, ISMP created and periodically updates a list of potential high-alert medications. During May and June 2014, practitioners responded to an ISMP survey designed to identify which medications were most frequently considered high-alert drugs by individuals and organizations. Further, to ensure relevance and completeness, the clinical staff at ISMP, members of the ISMP advisory board, and safety experts throughout the US were asked to review the potential list. This list of drugs and drug categories reflects the consensus thinking of all who provided input.

© ISMP 2014. Permission is granted to reproduce content with proper attribution for internal use within healthcare organizations. Other reproduction is prohibited without written permission from ISMP. Report actual and potential medication errors to the ISMP National Medication Errors Reporting Program (ISMP MERP) on its website (www.ismp.org) or by calling 1-800-FAIL-SAFE).

ISMP
www.ismp.org

- The Institute of Safe Medication Practices (ISMP) maintains lists of "high-alert" medications that have potential for increased risk of harm if used incorrectly.[1]
- High-alert medications merit special safeguards to reduce the risk of errors, including standardizing the ordering, storage, preparation, and administration of these products.[1]
- Use of pre-mixed commercial CRRT products instead of pharmacy compounded fluids has been shown to reduce the risk of mixing errors and contamination.[2,3]

Dextrose, hypertonic, 20% or greater

Dialysis solutions, peritoneal and hemodialysis

Epidural or intrathecal medications

1. ISMP. Institute of Safe Medication Practices. List of high-alert medications. http://www.ismp.org/Tools/highalertmedications.pdf. accessed 2/5/2018;
2. Barletta et al. Pediatr Nephrol 2006 Jun;21(6):842-5;
3. Flynn et al. Am J Health Syst Pharm 1997 May 1;54(9):1110.

Commercial CRRT Solutions Are Associated with Fewer Preparation Errors

- Comparison of CRRT medication errors in manually-compounded vs. commercially-available solutions
- Internet based survey of clinicians across more than 100 programs; 31 programs responded
- 18 of 31 programs (58%) reported at least one error (2 anticoagulation, 16 solution compounding)
- 89% (16/18) of reported CRRT solution errors were due to compounding
- ALL errors occurred in manually-prepared solutions; 0 errors were observed in commercial solutions
- 56% of compounding errors resulted in patient harm

Compounding Errors (N=16)

	Manually Compounded	Commercial Solution	P
Dialysate	9	0	0.005
Replacement	7	0	0.051
Total # Errors	16	0	<0.001

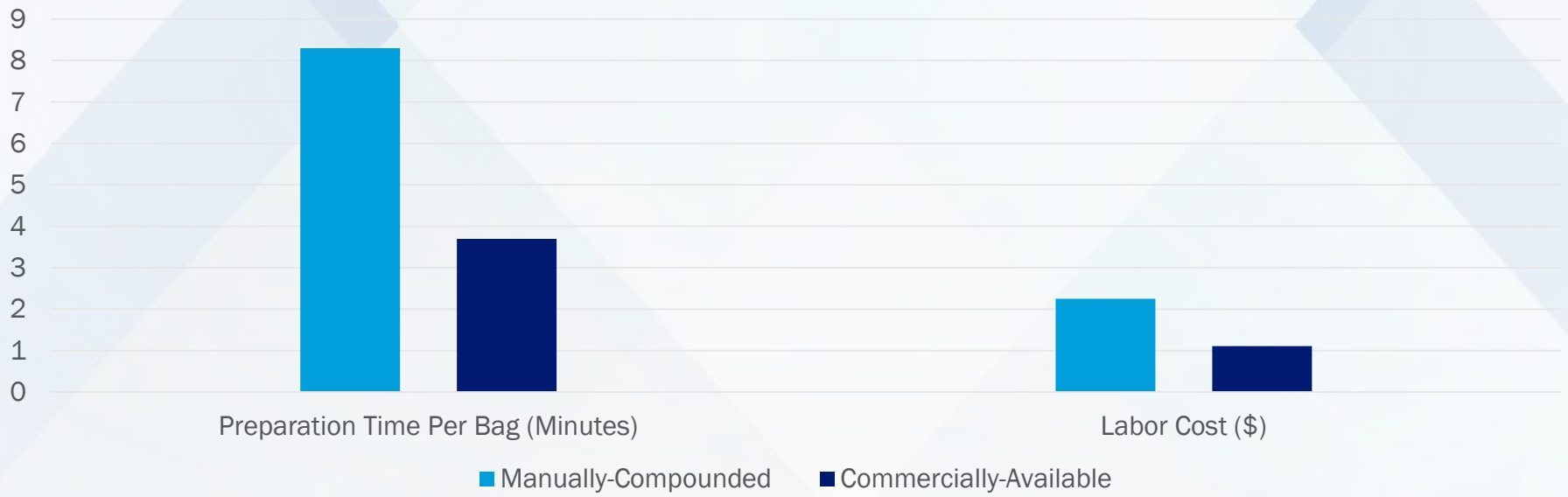
Level of Harm Resulting from Errors (N=16)

	Number (%) Errors	Harm Description
Error, No Harm	7 (44%)	N/A
Error, Harm	6 (38%)	Seizures related to hyper/hyponatremia
	1 (6%)	Cardiac arrest
Error Death	2 (12%)	Patient death

Barletta et al. Pediatr Nephrol 2006 Jun;21(6):842-5.

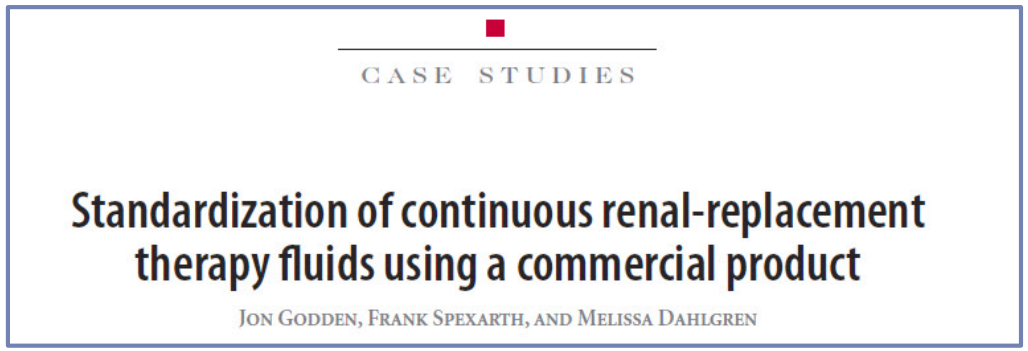
Commercially-Available CRRT Decreased Resource Utilization

- Manually compounding CRRT solutions can be extremely labor intensive, given a single patient can often require ≥50L of dialysis solutions per day
- Preparation times and labor costs were reduced by 50% after converting from manual compounding to commercially available CRRT solutions



Barletta et al. Hospital Pharmacy 2008.;43:329-34.

Routine Use of Pre-Made CRRT Solutions Yields Significant Cost Savings


CASE STUDIES

Standardization of continuous renal-replacement therapy fluids using a commercial product

JON GODDEN, FRANK SPEXARTH, AND MELISSA DAHLGREN

- Quality improvement initiative undertaken by a large hospital to increase standardization of CRRT fluids and practices
- Average of 200 CRRT patients annually
- Use of the commercial product reduced the need for pharmacy compounding of CRRT fluids by more than 80%
- Total estimated savings due to reduced labor and product costs during the first 6 months following conversion was $399,290

Table 1.
Estimated Cost Savings Achieved Through Conversion to a Commercial Fluid Product[a]

Year	Total CRRT Fluid Volume (L)[b]	No. CRRT Fluid Bags Prepared[b]	Product Cost ($)[c]	Technician Labor Cost ($)[d]
2007	87,452	21,863	646,729	394,200
2009	92,464	20,656	444,539	197,100
Cost savings			202,190	197,100

[a]CRRT = continuous renal-replacement therapy.

[b]After the addition of electrolytes to commercial 3.6-L bags of sterile water, sterile water was added to provide a total volume of 4 L.

[c]Includes both commercial and pharmacy-compounded bags.

[d]Estimated wages plus benefits, assuming the elimination of one full-time technician (24-hour, year-round coverage) from the process of preparing CRRT fluids.

Godden et al. Am J Health Syst Pharm 2012 May 1;69(9):786-93.

Conclusions

- Periodic drug shortages continue to challenge patient care
- Critical Care products are particularly impacted by shortages
- Compounding errors, reliance on alternative medications and treatment delays resulting from drug shortages adversely affect patient outcomes
- Reducing the complexity of IV solution preparation leads to fewer medication errors
- Dialysis solutions are “high-alert” medications that benefit from standardized preparation
- Studies have shown the potential risk of error increases when a high volume of dialysis solutions are compounded manually
- Standardized, pre-made CRRT solutions have shown to be less prone to preparation errors, may improve resource utilization and reduce costs
- Patient safety and efficiency of CRRT may benefit from routine utilization of commercially-available, pre-made solutions may benefit patient safety and efficiency

Baxter

Thank You

Baxter is a registered trademark of Baxter International Inc.
Any other trademarks, product brands or images appearing herein are the property of their respective owners.
USMP/MG3/18-0001(1) 05/19