UK research project on Ready-to-Administer IVP Medicines

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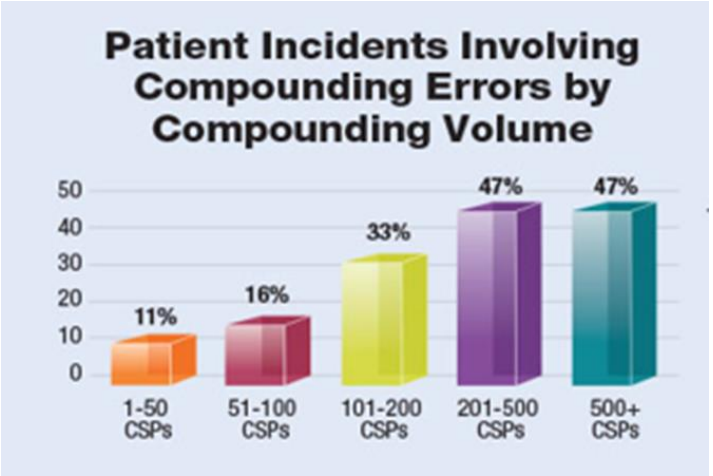
Examples of IV Drug Delivery Systems

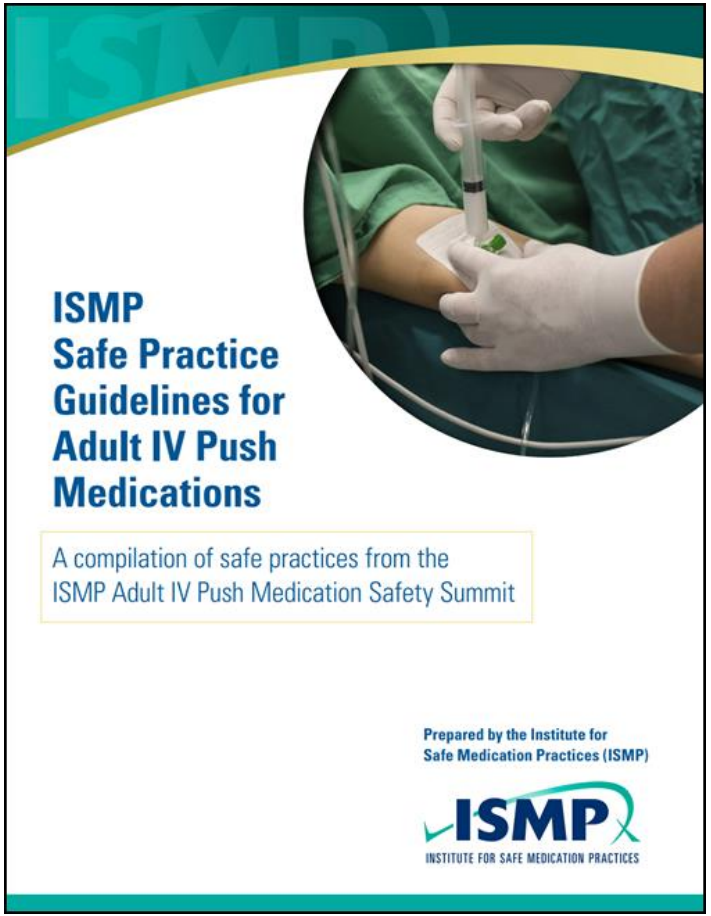
Delivery System	Examples
Manufacturer ready-to-use	Medications from the original manufacturer
Outsourced ready-to-use	Outsourced medications from companies registered with USFDA as 503b “registered outsourcing facilities”
Point-of-care activated	Mini-bag Plus® ADDVantage® products
Pharmacy compounded	Compounding medications in the pharmacy department
Non-pharmacy compounded at point-of-care	Compounding medications on nursing units
Ready-to-administer	Simplist™ prefilled syringes

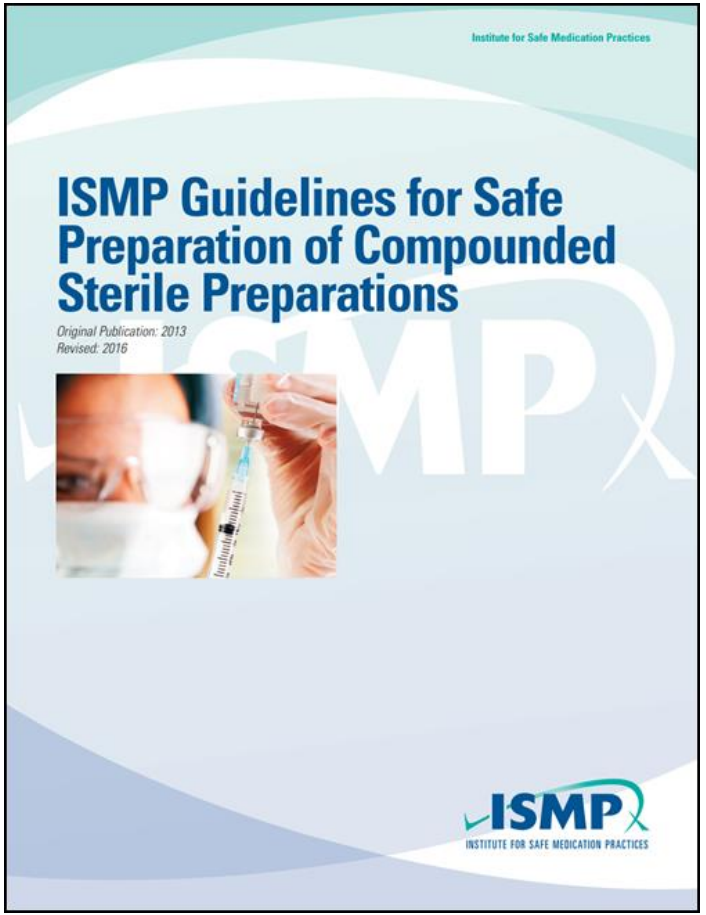
Sterile Compounding Errors and Harm

- Significant patient harm related to sterile compounding continues to occur in the United States and globally
- Data submitted to the ISMP National Medication Errors Reporting Program (MERP) has repeatedly shown manual inspection of IV admixture ingredients is an inadequate deterrent in preventing preparation and dispensing errors



10th Annual National Survey State of Pharmacy Compounding 2017, Pharmacy Purchasing & Products April 2017:s4-52.


ISMP
Safe Practice Guidelines for Adult IV Push Medications
A compilation of safe practices from the ISMP Adult IV Push Medication Safety Summit
Prepared by the Institute for Safe Medication Practices (ISMP)
ISMP
INSTITUTE FOR SAFE MEDICATION PRACTICES


Institute for Safe Medication Practices
ISMP Guidelines for Safe Preparation of Compounded Sterile Preparations
Original Publication: 2013
Revised: 2016
ISMP
INSTITUTE FOR SAFE MEDICATION PRACTICES

ISMP Surveys on IV Push Practices

2010

- **Survey: Impact of the economic crisis/shortages on medication safety**
  - Increase in nurses preparing or manipulating parenteral medications on the clinical unit

2012

- **Survey: Practices when using CARPUJECT prefilled medication syringes**
  - Withdrawing medication from prefilled syringe cartridges

2014

- **Survey: IV push practices**
  - Unnecessary dilution of dispensed ready-to-administer medications
  - Inappropriate use of prefilled saline flush syringes for dilution

2018

- **Survey: IV push practices**
  - Follow up to understand current practices associated with IV push medications
  - Determine if ongoing drug shortages and teaching strategies around this critical skill have impacted current practices

First Consensus Development Conference - 1999

- Evaluated the relative safety of (non-electronic) drug delivery systems then available
- Decision-analysis method ranked 6 systems
  - Safety, cost, simplicity-of-use, and training required
- Highest scored: **manufacturer-prepared**, point-of-care activated, and pharmacy-based admixture systems
- The requirement for a combination of systems was discussed
  - Lack of availability of highly rated systems

Schneider PJ. A review of the safety of intravenous drug delivery systems. Hosp Pharm. 1999;34(9):1044-1056.

Second Consensus Development Conference – 2008

- Ranked 5 systems, noting few major developments in availability of systems
  - Applicability, ease-of-use, regulatory compliance, cost, safety, and resources required
- **Manufacturer-prepared** ranked highest again
- Panel noted the complexity of IV medication delivery had increased
  - No single system meets all needs and situations

Sanborn MD, Moody ML, Harder KA, et al. Second consensus development conference on the safety of intravenous drug delivery systems-2008. Am J Health Syst Pharm. 2009;66: 185-192.

IV Drug Delivery Since 2008…

- Regulatory and standards changes
  - Continued revisions to USP <797> and <800>
  - Updates to National Patient Safety Goals
  - Passage of the 2013 Drug Quality and Security Act
  - Standardize for Safety
- Development and expansion of technology
  - IV workflow, interoperability and automation
  - Robotics
- Clinical challenges
  - Drug shortages
  - Pricing and access
  - Pandemic-related (e.g. staffing)

Rodriguez R. The safety of intravenous drug delivery systems: update on current issues since the 2009 Consensus Development Conference. Hosp Pharm. 2018.

Comparing Practice Over Time

Table 2. Results from Preconference Survey Statements Specific to the 2018 Conference

Statement	No. (%) Who Agree in 2018 (*n* = 31)
My hospital has experienced a disruption of supply from manufacturer[illegible]tsourced (503B) compounding entities.	30 (97)
My hospital has a proactive system in place to identify and mitigate d[illegible]n of i.v. products.	11 (35)
My hospital uses an automated i.v. workflow management system [illegible]ove the safety and efficiency of the medication use process.	11 (35)
My institution consistently uses electronic health record operab[illegible]erface between the i.v. pump and the electronic health record.	6 (19)
The majority of US hospitals have a complete understanding of the various factors that contribute to the cost-effectiveness of delivering safe i.v. admixtures to patients (i.e., product and staffing waste).	0 (0)

Gabay M, Hertig JB, Degnan D, Burger M, Yaniv A, Mclaughlin M, Lynn Moody M. Third Consensus Development Conference on the Safety of Intravenous Drug Delivery Systems-2018. Am J Health Syst Pharm. 2020 Jan 24;77(3):215-220. doi: 10.1093/ajhp/zxz277. PMID: 31811297.

Key Survey Observations

- Respondents suggest IV admixture use is safer than 5 years ago
  - 90% agree, improving from 76% in 2008
- 97% of respondents experienced a supply disruption
  - 81% experienced a patient safety event related to a disruption
- 45% agree outsourcing IV admixtures is cost-effective (59% in 2008)
  - No respondents (0%) had a complete understanding of factors that contribute to cost-effectiveness

Gabay M, Hertig JB, Degnan D, Burger M, Yaniv A, Mclaughlin M, Lynn Moody M. Third Consensus Development Conference on the Safety of Intravenous Drug Delivery Systems-2018. Am J Health Syst Pharm. 2020 Jan 24;77(3):215-220. doi: 10.1093/ajhp/zxz277. PMID: 31811297.

Third Consensus Development Conference

- Participants/Process
- Statements:

(1) Healthcare institutions should promote a culture of i.v. drug delivery safety across all sites of care that is patient-centric and proactive

(2) Organizational leadership is accountable for ensuring the highest level of safety regarding i.v. drug delivery systems

(3) Manufacturer-prepared products are the safest i.v. drug delivery system, and manufacturer-prepared, ready-to-administer products are preferred for patient use whenever possible

(4) Compounding sterile preparations is a high-risk practice, and incorporating established standards, such as USP chapter 797, is essential to ensure benefit while reducing risks to the patient

(5) All non-pharmacy compounding should be restricted to only immediate-use, urgent situations

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Third Consensus Development Conference

6) Specialized education, training, certification, and competency with regard to compounding of sterile preparations should be required for pharmacists, pharmacy technicians, and other involved healthcare providers

(7) Automation and technology that have been validated to improve the safety of CSPs should be implemented

(8) The profession of pharmacy must take the lead in interdisciplinary efforts for the safety of i.v. drug delivery systems

(9) A legislative and regulatory framework that supports and encourages i.v. medication safety in all settings should be developed

(10) the organizational costs of inaction, or of pursuing the minimum action necessary with regard to the safety of i.v. drug delivery, far exceed an institutional financial investment in the safest systems for the patient and staff

- Better understanding “costs of inaction” and “holistic costs is vital

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Past Research

SPECIAL FEATURE

Third Consensus Development Conference on the Safety of Intravenous Drug Delivery Systems—2018

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Mary Lynn Moody, B.S.Pharm., University of Illinois at Chicago College of Pharmacy, Chicago, IL.

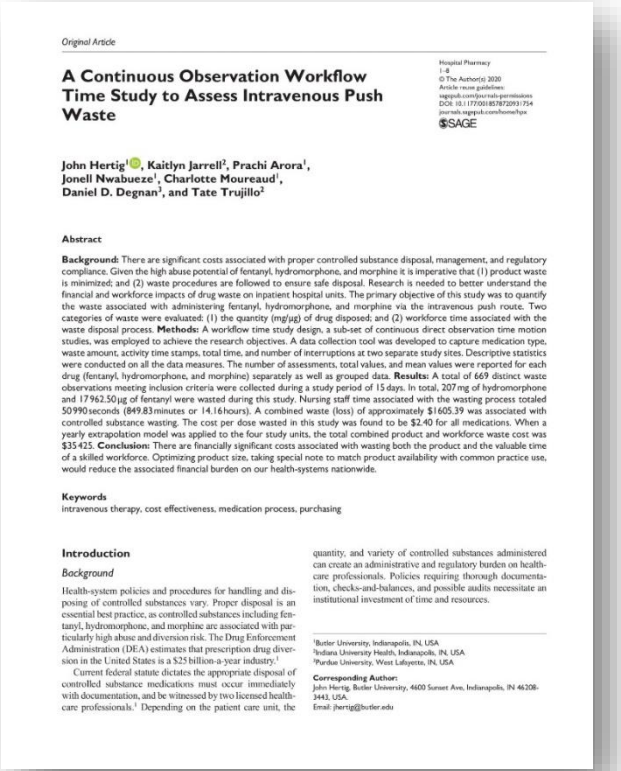
Purpose. The Third Consensus Conference on the Safety of Intravenous Drug Delivery Systems was convened to evaluate the benefits and risks of available systems and assess ongoing threats to the safety of intravenous drug delivery.

Summary. The Third Consensus Conference on the Safety of Intravenous Drug Delivery Systems convened in Chicago, Illinois in November 2018. An expert panel of healthcare providers with experience in medication quality and safety, pharmacy and nursing operations, information technology, and/or sterile compounding led the conference. An experienced audience of approximately 30 healthcare leaders provided feedback to the panel via preconference survey and during the conference. Additionally, expert speakers presented on a range of issues, including the effects of drug shortages, the impact of standards and guidelines, and patient and administrator perspectives on the importance of intravenous drug delivery safety.

Conclusion. At the end of the conference, the expert panel concluded that manufacturer ready-to-use products remain the safest intravenous drug delivery system due to their many benefits and low overall risk profile. The panel identified various ongoing threats to the safety of intravenous drug delivery, with major concerns including the impact of drug shortages and lack of intravenous product standardization. Finally, the panel agreed upon a series of statements designed to advance the safety of intravenous drug delivery in healthcare institutions.

Keywords: drug administration, drug compounding, drug safety, intravenous infusion, pharmacy administration

Am J Health-Syst Pharm. 2020; 77:215-221



Original Article

A Continuous Observation Workflow Time Study to Assess Intravenous Push Waste

Hospital Pharmacy
1–8

DOI: 10.1177/0018578720937541
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SAGE

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Abstract

Background: There are significant costs associated with proper controlled substance disposal, management, and regulatory compliance. Given the high abuse potential of fentanyl, hydromorphone, and morphine it is imperative that (1) product waste is minimized; and (2) waste procedures are followed to ensure safe disposal. Research is needed to better understand the financial and workforce impacts of drug waste on inpatient hospital units. The primary objective of this study was to quantify the waste associated with administering fentanyl, hydromorphone, and morphine via the intravenous push route. Two categories of waste were evaluated: (1) the quantity (mg/µg) of drug disposed; and (2) workforce time associated with the waste disposal process. **Methods:** A workflow time study design, a sub-set of continuous direct observation time motion studies, was employed to achieve the research objectives. A data collection tool was developed to capture medication type, waste amount, activity time stamps, total time, and number of interruptions at two separate study sites. Descriptive statistics were conducted on all the data measures. The number of assessments, total values, and mean values were reported for each drug (fentanyl, hydromorphone, and morphine) separately as well as grouped data. **Results:** A total of 669 distinct waste observations meeting inclusion criteria were collected during a study period of 15 days. In total, 207 mg of hydromorphone and 17 962.50 µg of fentanyl were wasted during this study. Nursing staff time associated with the wasting process totaled 50 990 seconds (849.83 minutes or 14.16 hours). A combined waste (loss) of approximately $1605.39 was associated with controlled substance wasting. The cost per dose wasted in this study was found to be $2.40 for all medications. When a yearly extrapolation model was applied to the four study units, the total combined product and workforce waste cost was $35 425. **Conclusion:** There are financially significant costs associated with wasting both the product and the valuable time of a skilled workforce. Optimizing product size, taking special note to match product availability with common practice use, would reduce the associated financial burden on our health-systems nationwide.

Keywords
intravenous therapy, cost effectiveness, medication process, purchasing

Introduction

Background

Health-system policies and procedures for handling and disposing of controlled substances vary. Proper disposal is an essential best practice, as controlled substances including fentanyl, hydromorphone, and morphine are associated with particularly high abuse and diversion risk. The Drug Enforcement Administration (DEA) estimates that prescription drug diversion in the United States is a $25 billion-a-year industry.[1]

Current federal statute dictates the appropriate disposal of controlled substance medications must occur immediately with documentation, and be witnessed by two licensed healthcare professionals.[1] Depending on the patient care unit, the quantity, and variety of controlled substances administered can create an administrative and regulatory burden on healthcare professionals. Policies requiring thorough documentation, checks-and-balances, and possible audits necessitate an institutional investment of time and resources.

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Proposed Research in England

ORIGINAL ARTICLE

OPEN

A Comparison of Error Rates Between Intravenous Push Methods: A Prospective, Multisite, Observational Study

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Catherine R. Scott, CPHQ, Janelle R. Lenz, PharmD,**
*Xiaochun Li, PhD, MSc,† and Chelsea M. Anderson, PharmD, MBA, BCPS**

Objectives: Current literature estimates the error rate associated with the preparation and administration of all intravenous (IV) medications to be 9.4% to 97.7% worldwide. This study aims to compare the number of observed medication preparation and administration errors between the only commercially available ready-to-administer product (Simplist) and IV push traditional practice, including a cartridge-based syringe system (Carpuject) and vials and syringes.

Methods: A prospective, multisite, observational study was conducted in 3 health systems in various states within the United States between December 2015 and March 2016 to observe IV push medication preparation and administration. Researchers observed a ready-to-administer product and IV push traditional practice using a validated observational method and a modified data collection sheet. All observations were reconciled to the original medication order to determine if any errors occurred.

Results: Researchers collected 329 observations (ready to administer = 102; traditional practice = 227) and observed 260 errors (ready to administer = 25; traditional practice = 235). The overall observed error rate for ready-to-administer products was 2.5%, and the observed error rate for IV push traditional practice was 10.4%.

Conclusions: The ready-to-administer group demonstrated a statistically significant lower observed error rate, suggesting that use of this product is associated with fewer observed preparation and administration errors in the clinical setting. Future studies should be completed to determine the potential for patient harm associated with these errors and improve clinical practice because it relates to the safe administration of IV push medications.

and challenges with reversing pharmacologic effects of drugs administered by this route.[2] This risk is recognized by the medical community, and 99% of nurses agree that errors related to IV medication use pose a serious risk to patients.[1] In addition, many IV medications were identified as having a serious risk for patient harm on the high-alert medication list for acute care settings.[3]

A study in 2012 by Lahue et al[4] estimated that 1.2 million hospitalizations each year are impacted by preventable adverse drug events associated with injectable medications. Almost half (48%) of the errors that occur with all IV medications happen during preparation or administration,[1] but error rates related to these practices vary significantly in the literature. Studies worldwide estimate the error rate with all IV medications to be between 9.4% and 97.7%, with IV push administrations demonstrating higher error rates than IV infusions.[5–12] Common IV medication errors included failure to maintain aseptic technique during drug preparation, use of the wrong diluent, and incorrect labeling of an IV product.[5–12]

One of the factors associated with an increased potential for error with IV medications is the number of complex manipulations required when preparing and administering these drugs.[2,13] Drug manufacturers have begun to develop and market ready-to-administer IV push products with the aim of reducing this complexity of drug preparation and administration, while minimizing the potential for errors and patient harm. Ready-to-administer products are viewed as the IV drug delivery systems of choice,

Background

- Medication errors are common in an inpatient hospital setting adding to the healthcare burden – higher costs & increase in hospitalizations
- Most of the errors with intravenous (IV) medications are preparation and administration errors
  - Some cause adverse drug events which could lead to severe harm or are life-threatening.
- Use of RTA formulations could improve patient safety and efficiency and also reduce/eliminate waste in the system
- Past studies report lower errors rates with RTA but studies quantifying the cost savings produced by RTA formulations are limited
- Also, there is a scarcity of research comparing the drug waste with RTA and current compounding in a England health system

Background

- A cost minimization analysis study designed by Larmene 2019 compared the total costs of the conventional preparation method with RTA prefilled syringes using a Dutch health system, where the effectiveness parameter was reported as costs of the errors (obtained from Hug 2012)
- Another study by Cousins et al. conducted in UK Germany and France, reported preparation & administration error rates for aseptic compounding only
- A past study by Hertig et al., 2020 compared the opioid waste with the RTA and traditional vial and syringe method in US hospitals
- Reports suggest that the patterns of errors were similar in the US and UK hospitals, but the practice of pharmacy and nursing are reportedly different in the two countries

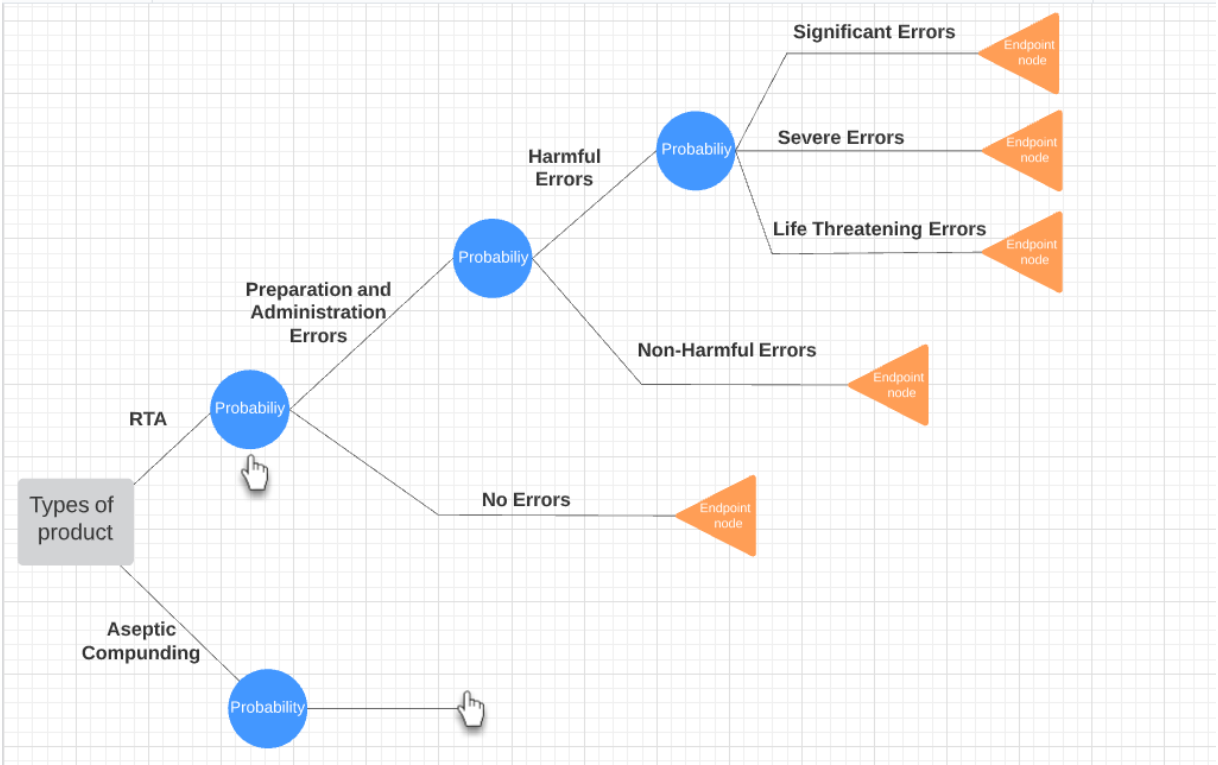
Proposed Aims

- **Aim 1**:
  - To compare the drug waste of RTA formulations and current compounding practices in inpatient settings in England
- **Aim 2**:
  - To develop a cost effectiveness (CEA) model comparing the RTA formulation to traditional compounding in an inpatient setting from the Hospital/NHS England perspective
  - In order to develop the CEA model, the input parameters will be obtained from past published studies conducted in similar settings
    - Different categories of the input parameters are outlined on next slide

Possible Sources to Obtain Inputs

Parameters	RTA	Traditional aseptic compounding
Costs		
Cost of the drug ($)	Provided by the Manufacturer	Provided by the Manufacturer
Cost associated with the preparation of drugs ($)	Berger and Degnan, 2019[10]	Berger and Degnan, 2019[10]
Cost associated with the administration of drugs ($)	Hertig et al., 2018[11]	Hertig et al., 2018[11]
Cost of the drug waste ($)	***Missing***	***Missing***
Cost associated with preparation and administration errors ($)	Hug 2012[12]	Hug 2012[12]
Probabilities		
Probability of administering the drug (Gentamycin, Insulin, Fentanyl)	***Missing***	***Missing***
Probability of preparation and administration errors per observation	Hertig et al., 2018[11]	Hertig et al., 2018[11]
Probability of errors leading to harm (or ADE)	Hug 2012[12]	Hug 2012[12]
Probability of errors categorized by severity	Hug 2012[12]	Hug 2012[12]
Effectiveness or Payoffs		
Errors at the end of each arm	Hertig et al., 2018[11]	Hertig et al., 2018[11]

Decision Tree Example



Key Takeaways: Optimizing Care Delivery

- Respondents suggest IV admixture use is safer today than 5 years ago; risks remain
  - Manufacturer-prepared, ready to administer products are preferred whenever possible
- Better understanding of the total cost of delivering safe IV drug therapy is needed!
  - “Total cost of care”
  - Product
  - Workforce
  - Other waste

Improved patient experience

Prioritizing nursing time

Ensuring patient safety

Establishing a compliant practice

Questions?


thank you
danke
謝謝
ngiyabonga
teşekkür ederim
gracias
merci
obrigado
bedankt
dziękuję
go raibh maith agat
mochchakkeram
sukriya
kop khun krap
terima kasih
arigatô
dakujem
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References

1) Lahue BJ, Pyenson B, Iwasaki K, Blumen HE, Forray S, Rothschild JM. National Burden of Preventable Adverse Drug Events Associated with Inpatient Injectable Medications: Healthcare and Medical Professional Liability Costs. *Am Health Drug Benefits*. 2012;5(7):1-10.
2) Taxis K, Barber N. Ethnographic study of incidence and severity of intravenous drug errors. *BMJ*. 2003;326(7391):684. doi:10.1136/bmj.326.7391.684
3) Taxis K, Barber N. Incidence and severity of intravenous drug errors in a German hospital. *Eur J Clin Pharmacol*. 2004;59(11):815-817. doi:10.1007/s00228-003-0689-9
4) Parshuram CS, To T, Seto W, Trope A, Koren G, Laupacis A. Systematic evaluation of errors occurring during the preparation of intravenous medication. *CMAJ*. 2008;178(1):42-48. doi:10.1503/cmaj.061743
5) Larmené-Beld KHM, Spronk JT-, Luttjeboer J, Taxis K, Postma MJ. A Cost Minimization Analysis of Ready-to-Administer Prefilled Sterilized Syringes in a Dutch Hospital. *Clin Ther*. 2019;41(6):1139-1150. doi:10.1016/j.clinthera.2019.04.024
6) Cousins DH, Sabatier B, Begue D, Schmitt C, Hoppe-Tichy T. Medication errors in intravenous drug preparation and administration: a multicentre audit in the UK, Germany and France. *BMJ Quality & Safety*. 2005;14(3):190-195. doi:10.1136/qshc.2003.006676
7) Hertig J, Jarrell K, Arora P, et al. A Continuous Observation Workflow Time Study to Assess Intravenous Push Waste. *Hospital Pharmacy*. 2020:0018578720931754
8) Blandford A, Dykes PC, Franklin BD, et al. Intravenous Infusion Administration: A Comparative Study of Practices and Errors Between the United States and England and Their Implications for Patient Safety. *Drug Saf*. 2019;42(10):1157-1165. doi:10.1007/s40264-019-00841-2
9) Brock TP, Franklin BD. Differences in pharmacy terminology and practice between the United Kingdom and the United States. *American Journal of Health-System Pharmacy*. 2007;64(14):1541-1546. doi:10.2146/ajhp060444
10) Burger M, Degnan D. Comparative Safety, Efficiency, and Nursing Preference Among 3 Methods for Intravenous Push Medication Preparation: A Randomized Crossover Simulation Study. *J Patient Saf*. 2019;15(3):238-245. doi:10.1097/PTS.0000000000000269
11) Hertig JB, Degnan DD, Scott CR, Lenz JR, Li X, Anderson CM. A Comparison of Error Rates Between Intravenous Push Methods: A Prospective, Multisite, Observational Study. *J Patient Saf*. 2018;14(1):60-65. doi:10.1097/PTS.0000000000000419
12) Hug BL, Keohane C, Seger DL, Yoon C, Bates DW. The costs of adverse drug events in community hospitals. *The joint commission journal on quality and patient safety*. 2012;38(3):120-126.