RUTGERS HEALTH
School of Nursing
Nurse Anesthesiology Program

Preventing the Occurrence of Wrong-Route Medication Administration Among Patients Receiving Neuraxial Anesthesia Using Neuraxial Route-Specific Medication Administration Equipment: A Systematic Review

Russell Lynn Memorial Resident Lecture Series

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October 4, 2025

A Work in Progress

- This presentation is based on our DNP project at Rutgers University.

- We are currently in the implementation phase of the project.

- We would like to thank our committee members for guiding us this far:
    - ANES Faculty: Dr. Stephen Pilot
    - NEST Faculty: Dr. Cheryl Holly

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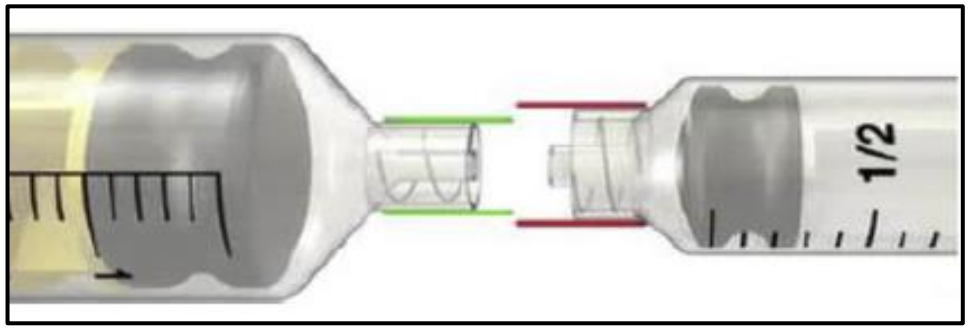
Objectives



Examine the following points regarding the significance of **non-Luer lock** connectors (ISO 80369-6; NRFit) for the safe administration of neuraxial anesthesia

- Background
- Significance
- Purpose
- Methodology
- Current phase of systematic review
- Anticipated results
- Dissemination of information

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Review Question

Compared to standard Luer lock connectors, to what extent can using neuraxial route-specific medication administration equipment prevent the occurrence of wrong-route medication administration errors among patients receiving neuraxial anesthesia?

Population	Patients receiving neuraxial anesthesia
Intervention	Neuraxial *route-specific* medication administration equipment (i.e., non-Luer lock connectors, specifically NRFit ISO 80369-6 connectors)
Comparison	Conventional standard of care; Luer lock syringes
Outcome	Prevention or reduction of wrong-route medication errors

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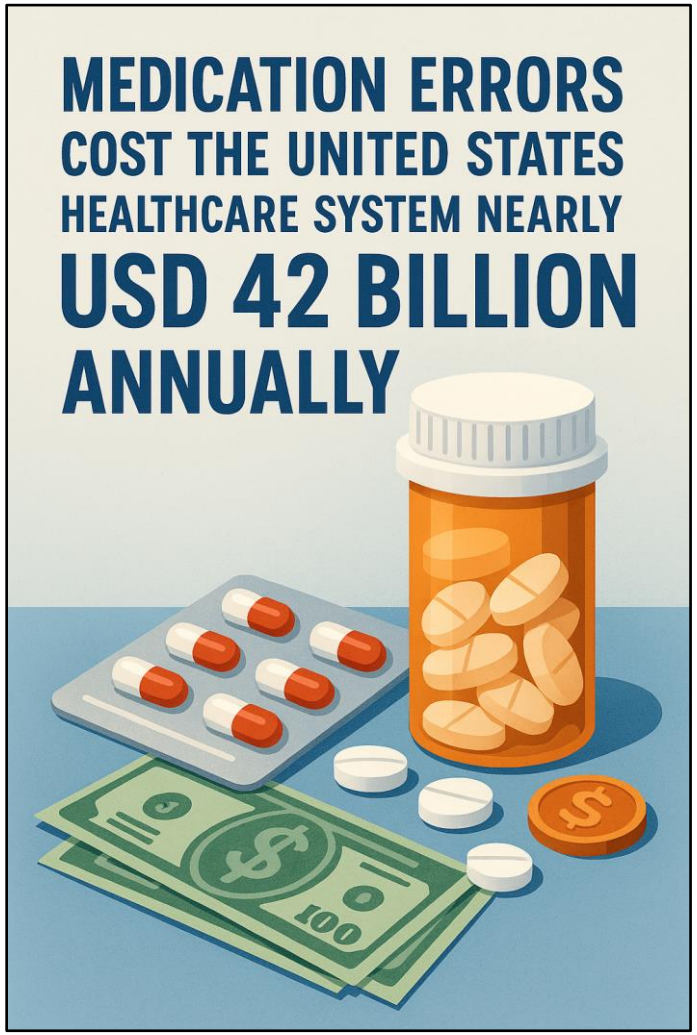
Background & Significance

Patient Safety Breach & Costs a lot of Money!

- Neuraxial anesthesia (spinal, epidural, & CSE) is commonly administered w/ standard Luer lock syringes, needles, & catheters
- Each year, **~ 3 million people <u>die</u>** from unsafe healthcare
  - ↳ Medication errors = **half** of these cases
- Medication-related harm affects **~ 1 in every 30** patients…
  - ↳ ***>25%** of this harm* = ***severe/life-threatening***
- ISO 80369-6 connectors ↓ **risk** of <u>misconnection</u> & unintended <u>wrong-route medication administration</u>
  - The physical differences b/w traditional Luer lock devices & non-Luer lock devices (ISO 80369-6;NRFit) render the equipment **<u>mechanically incompatible</u>**



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Neuraxial and peripheral misconnection events leading to wrong-route medication errors: a comprehensive literature review

Eugene R Viscusi ,[1] Vincent Hugo,[2] Klaus Hoerauf,[2,3] Frederick S Southwick[4]

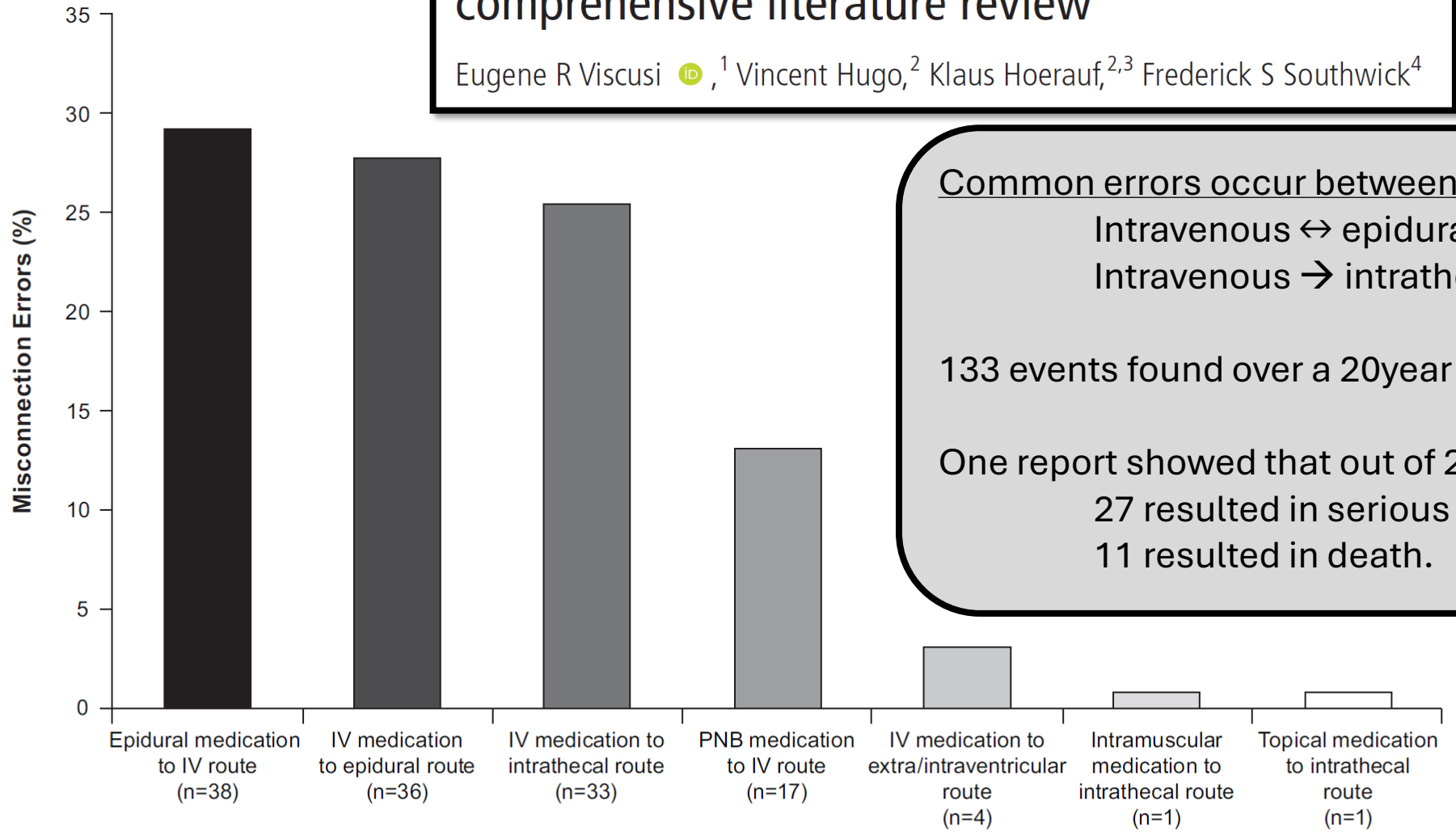

Figure 1 Neuraxial and peripheral nerve block misconnection errors identified in case reports (N=130) between 1999 and 2019. Intended route unknown for 3 of 133 cases. IV, intravenous; PNB, peripheral nerve block.

Common errors occur between administration of:

Intravenous ↔ epidural &
Intravenous → intrathecal

133 events found over a 20year period.

One report showed that out of 28 wrong route errors…

27 resulted in serious complications
11 resulted in death.

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Table 2 Individual drugs and other substances noted in a single case report involving neuraxial and peripheral misconnections, leading to wrong-route administration events

Drug type, name	Intended route of administration	Actual route of administration	Incident severity*
Antibiotics			
Cefotiam	Intravenous	IT	Moderate
Clindamycin	Intravenous	EPI	Low
Piperacillin-tazobactam	Intravenous	EPI	Moderate
Rifampicin	Intravenous	IT	Low
Chemotherapy			
Bleomycin	Intravenous	IT	Moderate
Doxorubicin	Intravenous	IT	Severe
Farmorubicin	Intravenous	IT	Death
PEG-asparaginase	Intramuscular	IT	Low
Contrast agents			
Diatrizoate meglumine	Intravenous	IT	Moderate
Iothalamate meglumine	Intravenous	IT	Moderate
Ioxaglate sodium	Intravenous	IT	Moderate
Ioxitalamate	Intravenous	IT	Moderate
Muscle relaxants			
Cisatracurium	Intravenous	EPI	Moderate
Pancuronium	Intravenous	EPI	Low
Opioids			
Hydromorphone	Intravenous	EPI	Moderate
Remifentanil	Intravenous	EPI	Low
Tramadol	Intravenous	IT	Death
Other			
Insulin	Intravenous	EPI	Moderate
Labetalol—beta blocker	Intravenous	IT	Low
Mercurochrome	TOP	IT	Severe
Neostigmine + atropine	Intravenous	EPI	Moderate
Parenteral nutrition	Intravenous	EPI	Moderate
Phenylephrine	Intravenous	EPI	Moderate
Phenytoin	Intravenous	ED	Moderate
Physostigmine (cholinesterase inhibitor)	Intravenous	IT	Low
Sodium chloride, ketorolac, esomeprazole, cefotaxime	Intravenous	EPI	Low

Background, cont.

GEDSA

ADVANCING PATIENT SAFETY

Global **E**nteral **D**evice **S**upplier **A**ssociation

Medical "tubing misconnections continue to cause severe patient injury and death, since tubes with different functions can easily be connected using Luer connectors, or connections can be "rigged" (constructed) using adapters, tubing or catheters"*.

The International Organization for Standardization (ISO) has developed the ISO 80369 series of small-bore medical connector standards to improve patient safety**.

These standards create unique tubing connectors for each bodily system that are mechanically incompatible outside of their therapeutic area. This reduces the risks of harmful and even fatal misconnections, where medical tubing inadvertently connects one bodily system to another.

Since 2013, GEDSA has collaborated with ISO

International Organization for Standardization

ISO

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ISO 80369 Series

80369-7,
Vascular/Intravenous
Published 2016

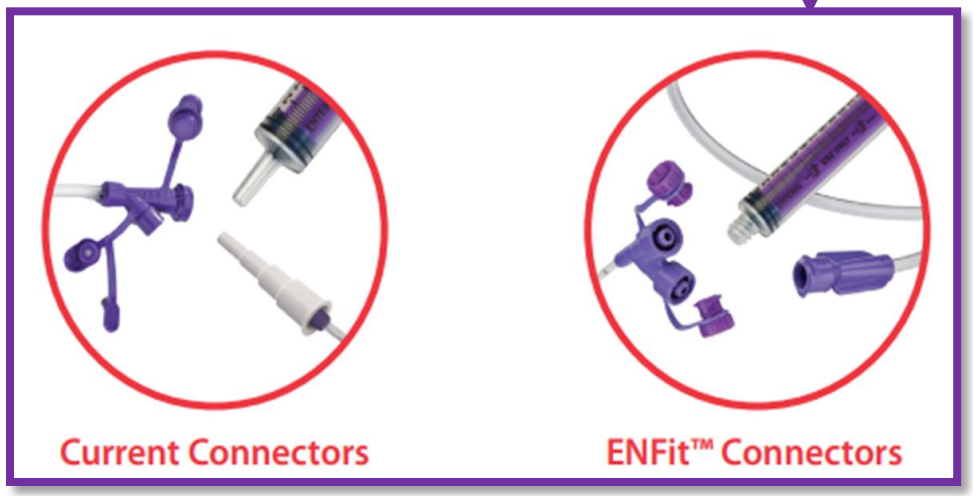
80369-5,
Limb Cuff Inflation
Published 2016

80369-4, Urinary Collection
Publication TBD

80369-6, Neuraxial
Published 2016

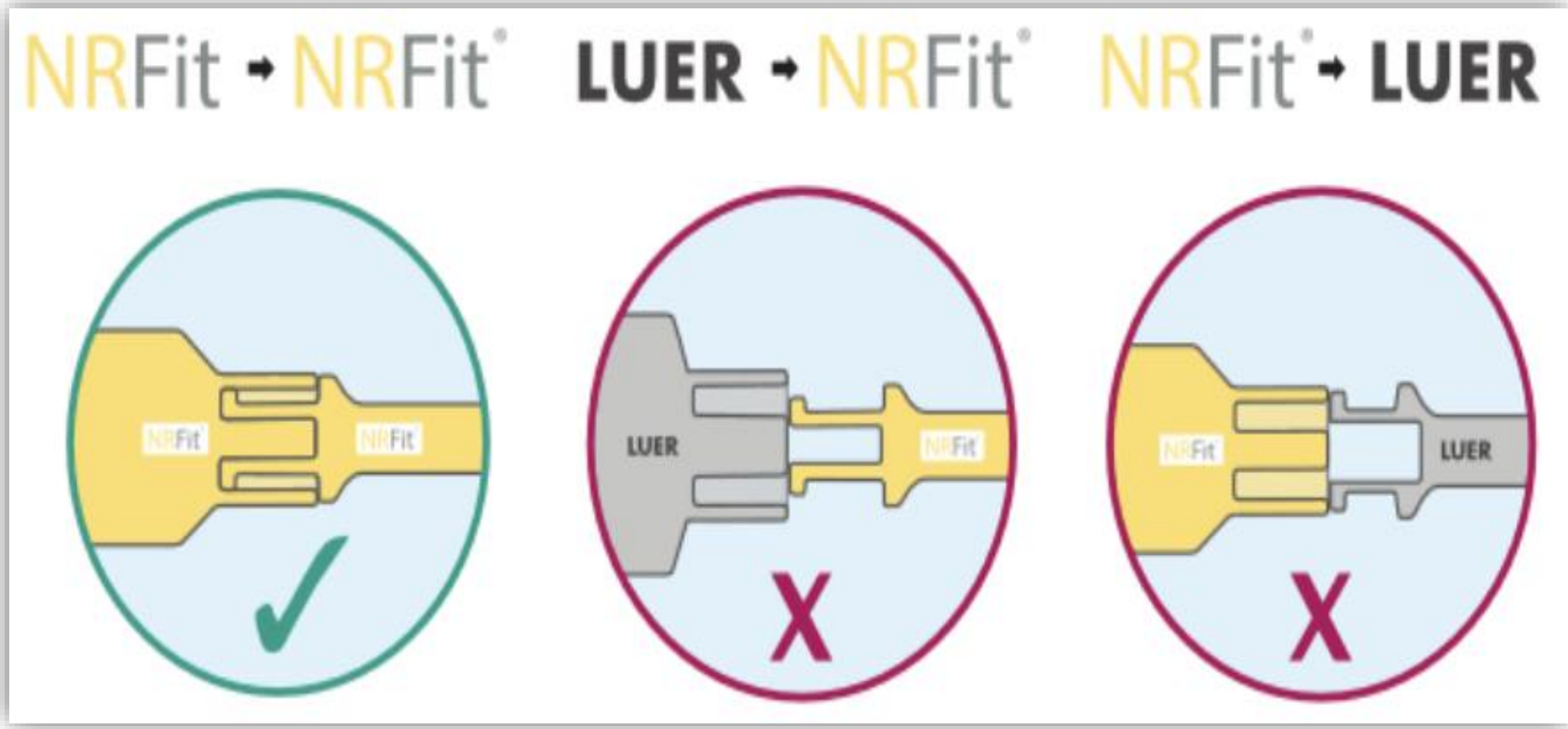
80369-2, Respiratory
Published 2016

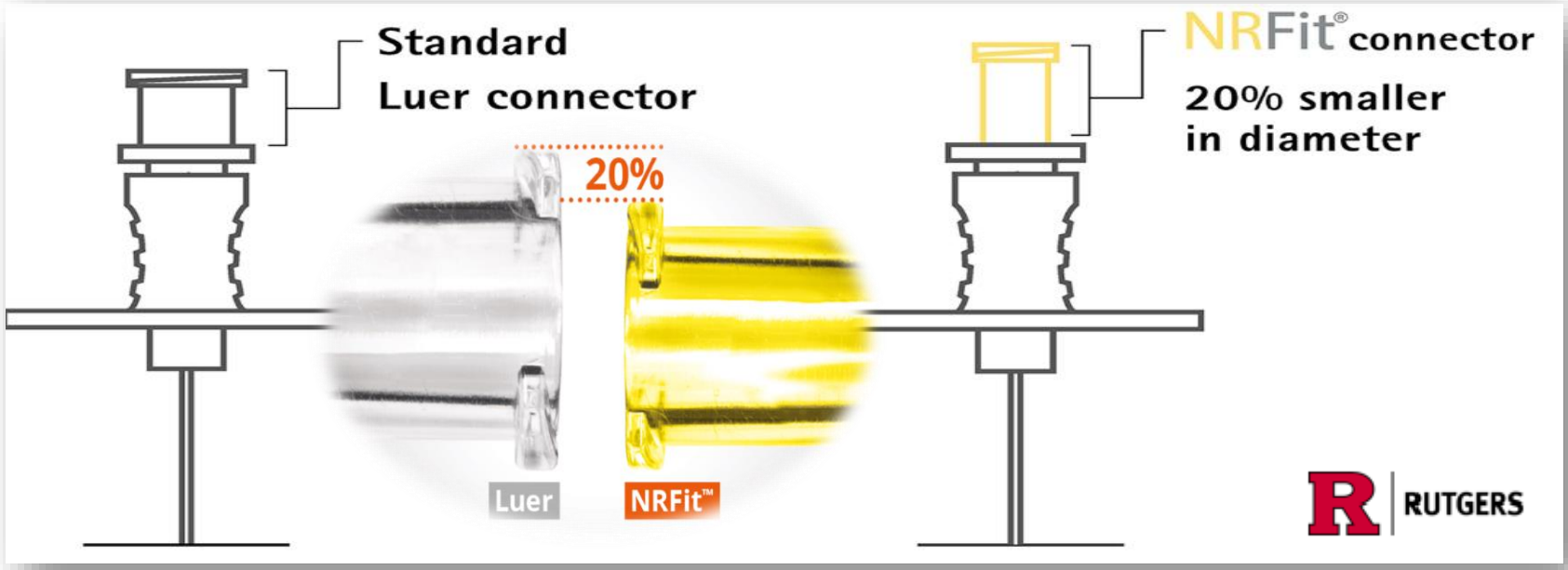
80369-3, Enteral
Published 2016

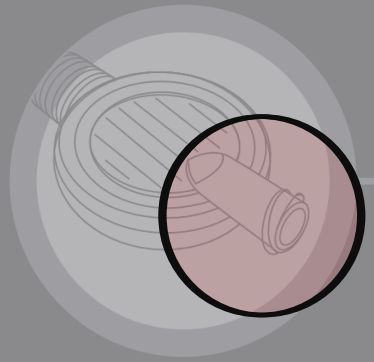


The Difference

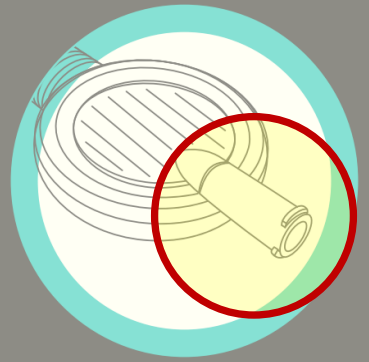
- 20% Smaller needle hub
- **Unique** threads on syringe
- Color Coded: Yellow







BACTERIAL FLAT FILTER



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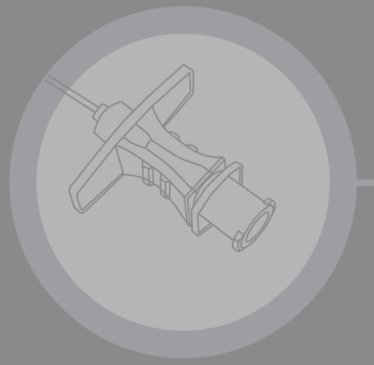
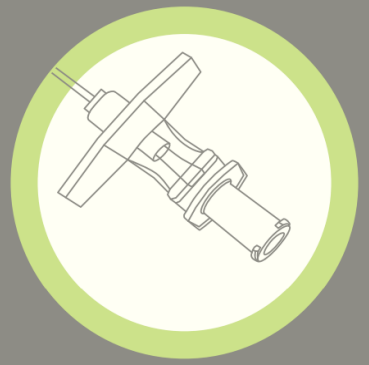


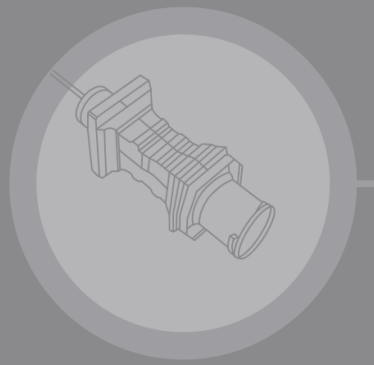
LUER

EPIDURAL NEEDLE

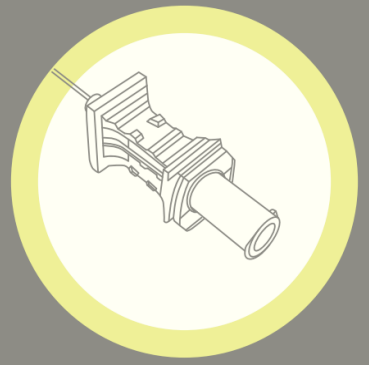
NRFit



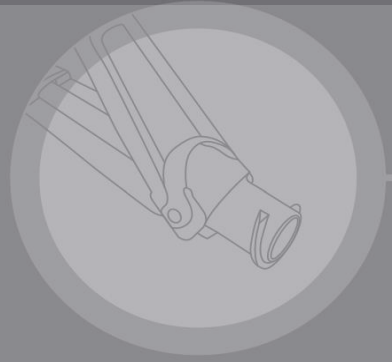
EPIDURAL NEEDLE



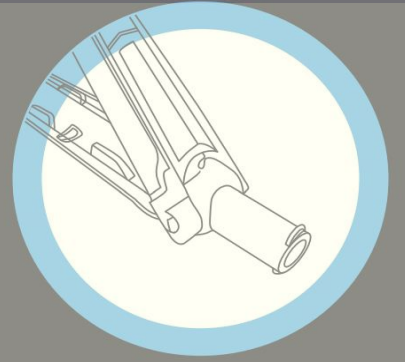
SPINAL NEEDLE



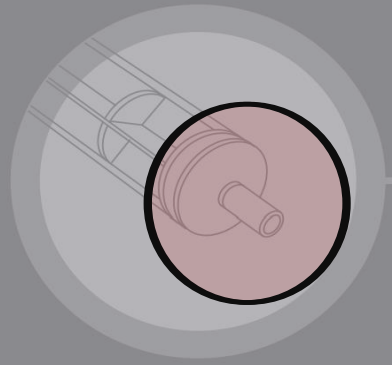
SPINAL NEEDLE



CATHETER CONNECTOR



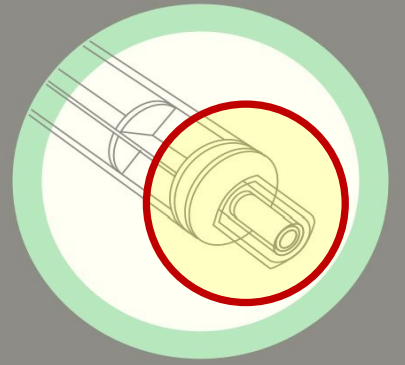
CATHETER CONNECTOR



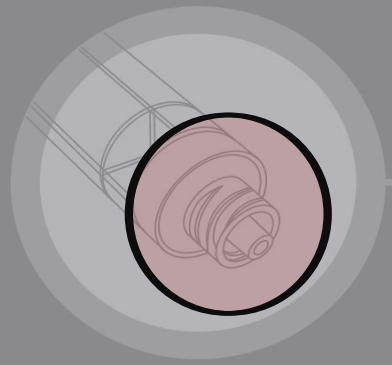
LUER

LUER SLIP SYRINGE

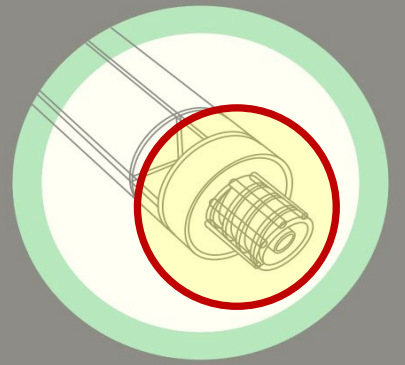
NRFit



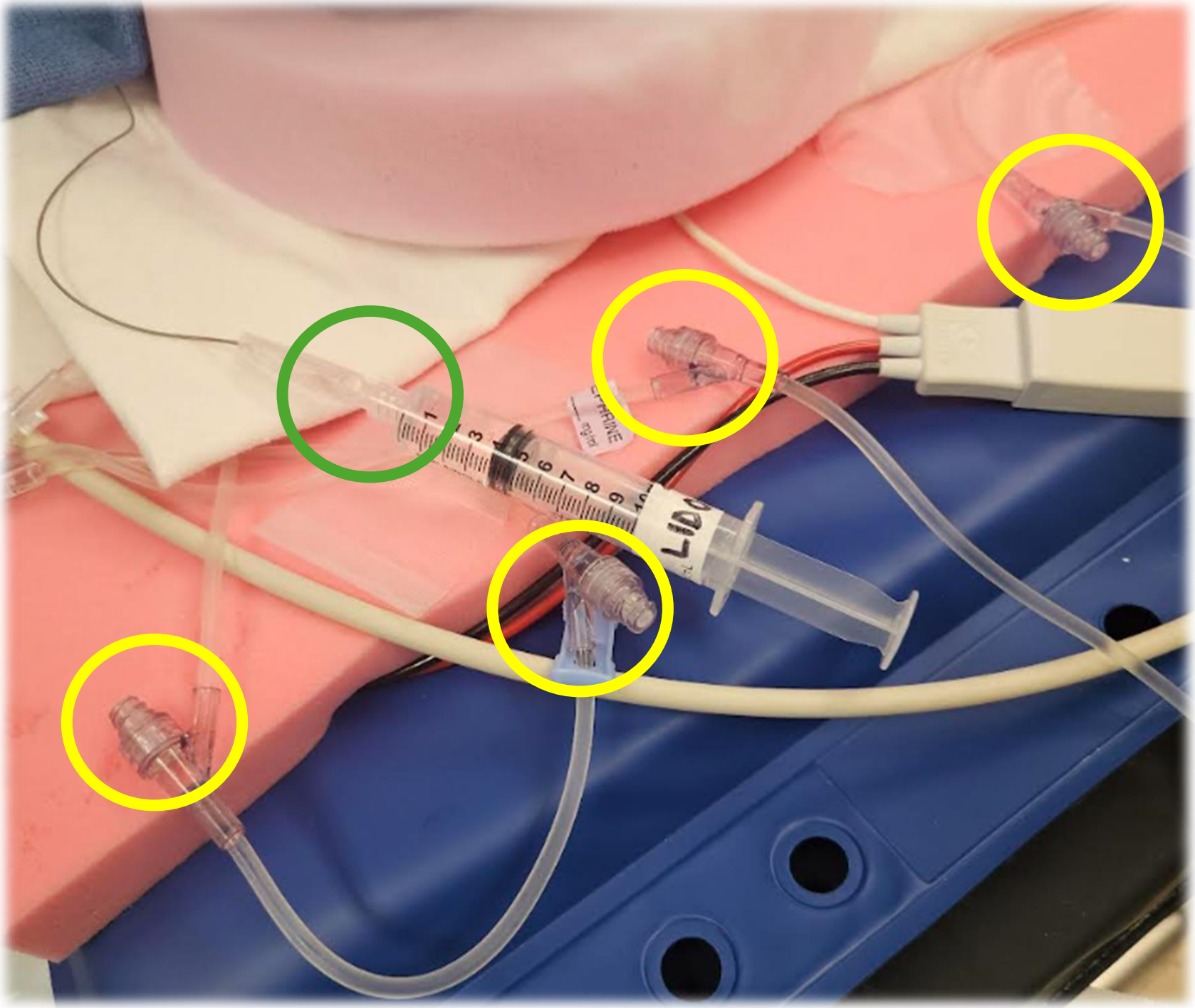
SLIP SYRINGE



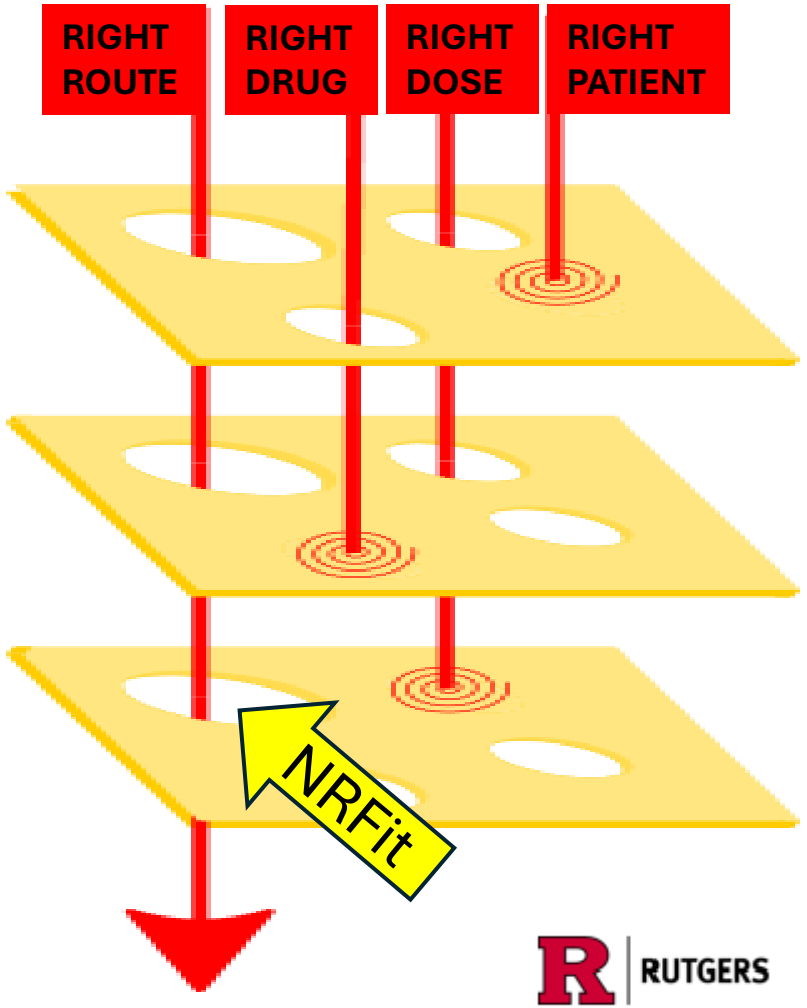
LUER-LOCK SYRINGE



LOCK TIP SYRINGE



Opportunity for ERROR!



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Purpose

This systematic review examines:

1. The **best available evidence** regarding the use of ***neuraxial route-specific medication administration equipment.***
   ↳ Specifically *ISO 80369-6; NRFit*
2. The effectiveness of *reducing or preventing wrong-route medication administration* via implementation of the NRFit system, compared to the currently used standard universal leur-lock type medication administration equipment.

Significance: Implementation of a *neuraxial route-specific* connection system will make tubing misconnections and wrong-route medication administration physically impossible, as the connector size and threads are mechanically incompatible with conventional Luer lock systems, resulting in *a decrease in medication administration errors and increased patient safety.*

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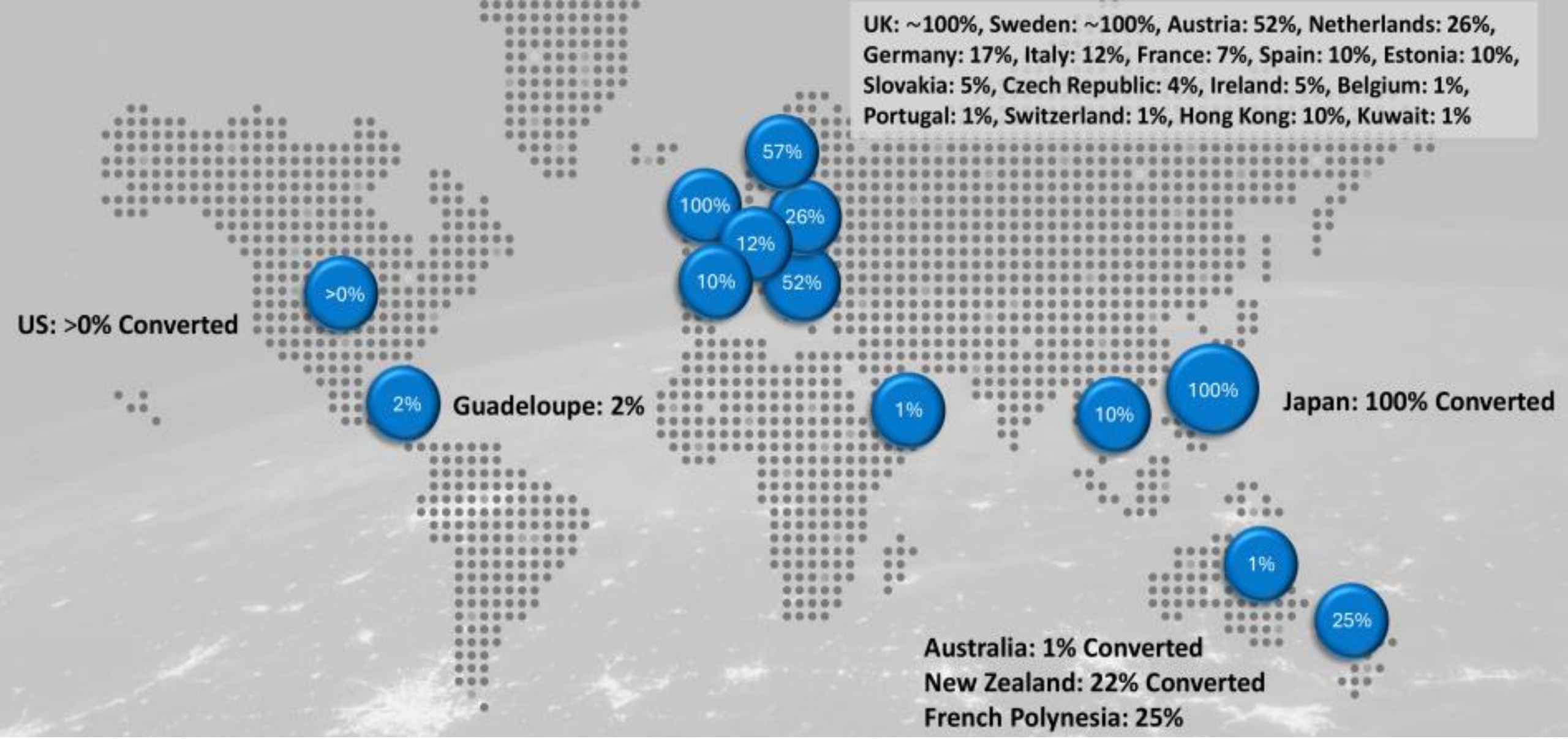

ISO 80369-6 is currently unavailable in the United States...

- Japan → first country to completely transition to NRFit devices in 2020;
  - ↳ Luer lock connection systems for the neuraxial route phased out of practice

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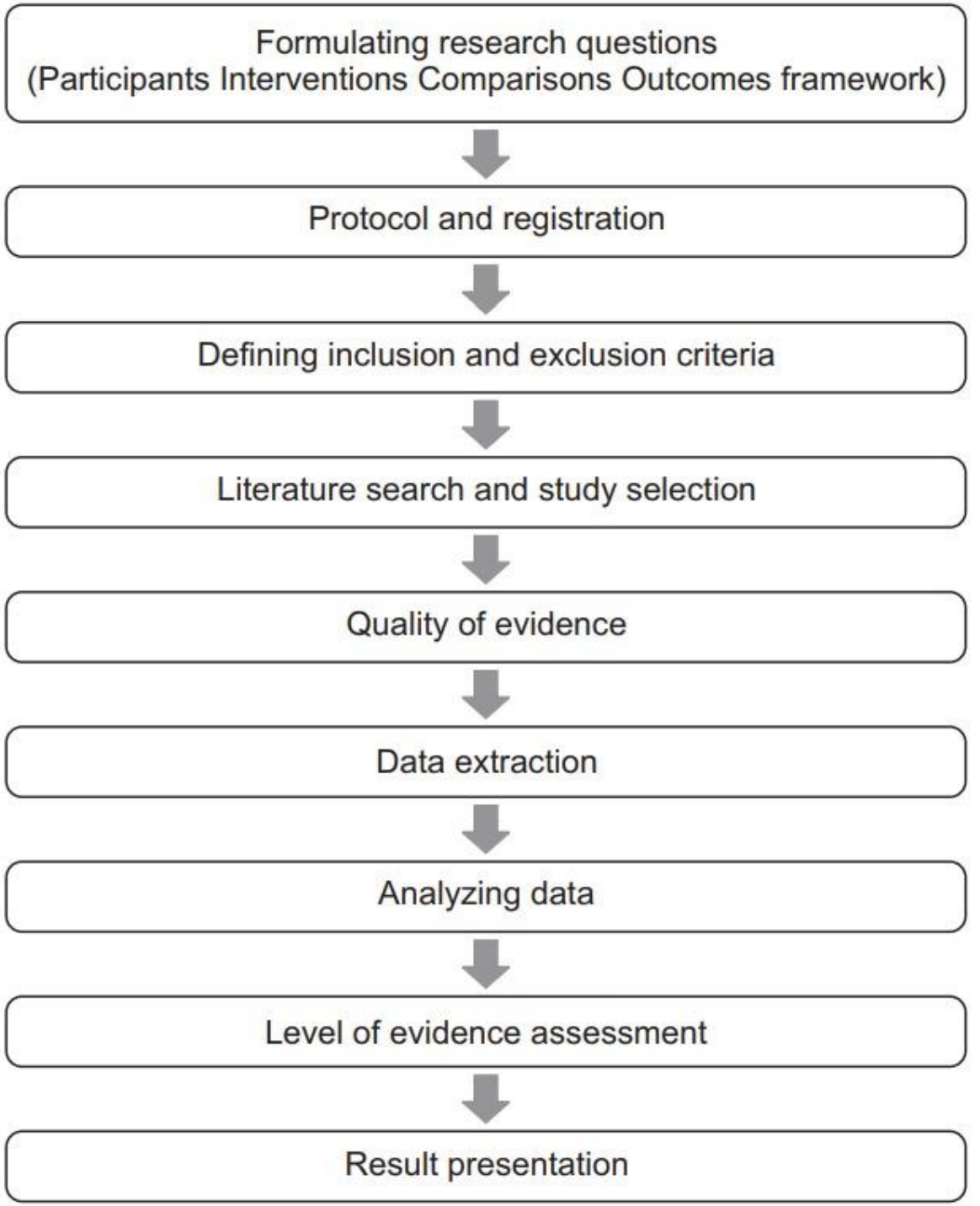
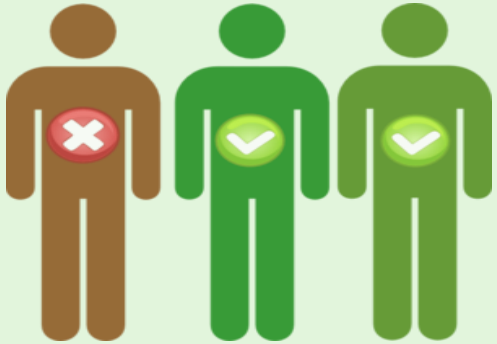
Methodology

- **Systematic review**: Synthesis of current evidence and a summary of results gathered from rigorously searching all available research using a clearly defined, systematic, objective, and reproducible approach to obtain an answer to a specific question.
- **Meta-analysis**: A statistical process employing scientific and objective analyses of combined results gathered from relevant research to identify trends, strengthen evidence, and resolve inconsistences across studies.
- A significant amount of data and clinical experience has been synthesized in countries such as Japan and the UK, where Healthcare systems have been fully converted to NRFit.
- There is l imited information regarding domestic details.
  - ↳ ISO 80369-6 is new to the US; 0% conversion.



Inclusion/Exclusion Criteria

Participants included:



- Age:18 years & older
- Gender: Any
- Ethnicity: Any

Interventions included:

- Patients must be receiving neuraxial anesthesia
  - Intrathecal and/or epidural
- Must utilize the ISO-80369-6 NRFit device or other non-Luer lock technology

Exclusion criteria:

- Patients < 18 years of age
- Patients *not* receiving neuraxial anesthesia

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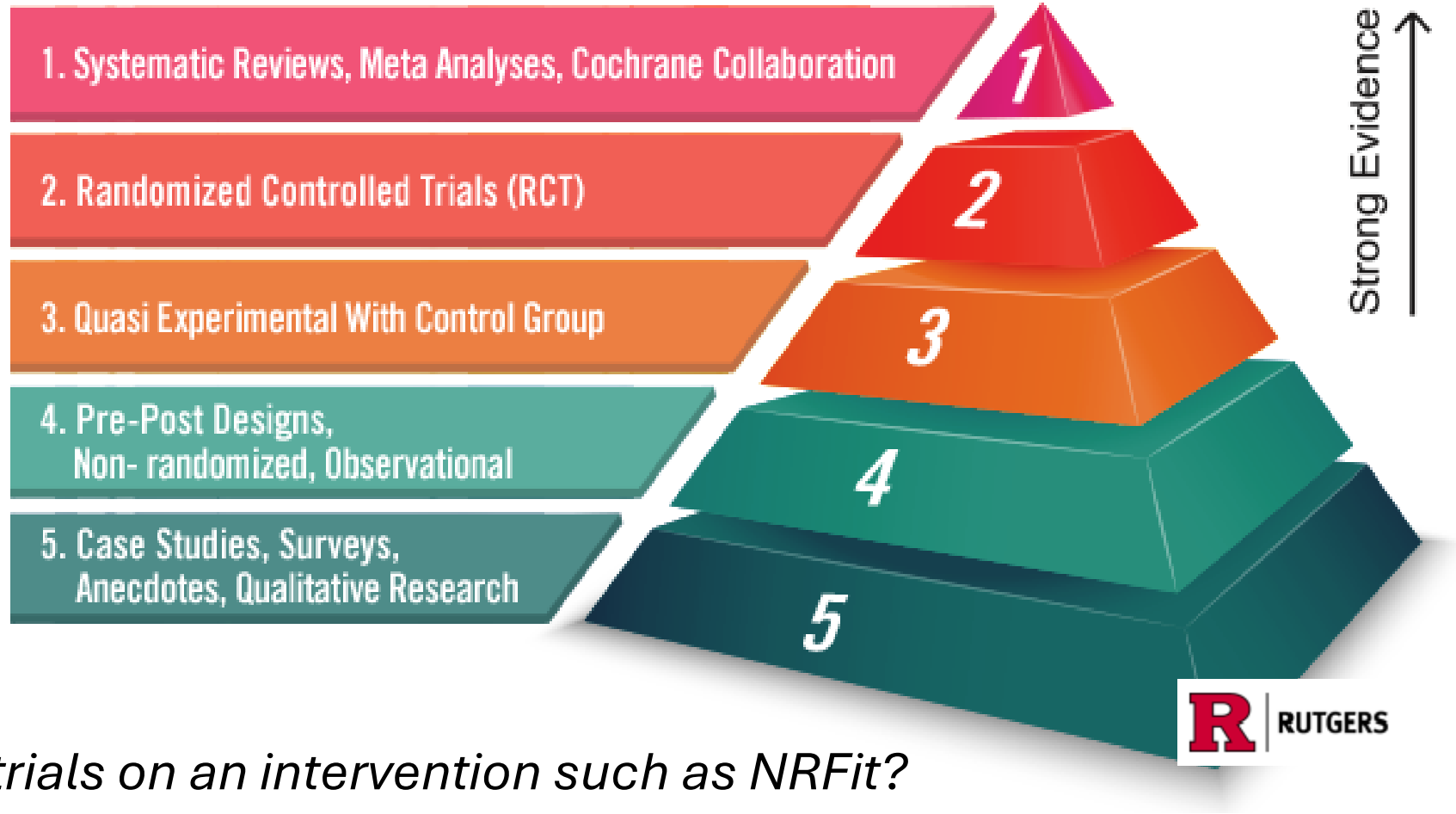
Types of Studies Included

- Peer-reviewed articles
- Published between 2013-2025
- Full-text, English language
- All levels of evidence accepted

- Randomized control trials are “Gold Standard”
  - Measures effectiveness of an intervention vs. a control
- Most of our evidence will likely be Lower-Level
  - Observational, Case-Studies, Anecdotes, & Qualitative Research
- WHY?



Is it ethical to perform clinical trials on an intervention such as NRFit?

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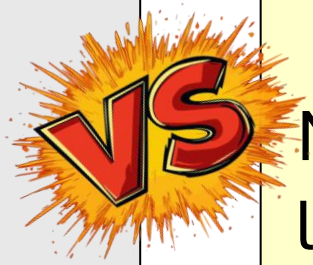
Control & Intervention

Control

Standard universal Luer lock systems



Intervention

Neuraxial-route-specific non-Luer lock systems (ISO 80369-6; NRFit)

Outcome Measure

Wrong-route medication administration rate

Either

Intravenous intention→ neuraxial administration

Or,

Neuraxial intention → intravenous administration

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Search Strategy

Databases accessed:

- **Cumulative Index to Nursing and Allied Health Literature (CINAHL)**
  - Access to quantitative & qualitative peer-reviewed journal articles, clinical trials, dissertations, and books related to nursing, allied health, and biomedical topics.
- **PubMed**
  - Access to **Medline** & the **National Library of Medicine (NLM)**
  - Includes peer reviewed journal articles and books
- **Excerpta Medica dataBASE (EMBASE)**
  - Access to research on pharmacology & **medical devices**
- **Wolters Kluwer**
- **National Institute of Health (NIH)**

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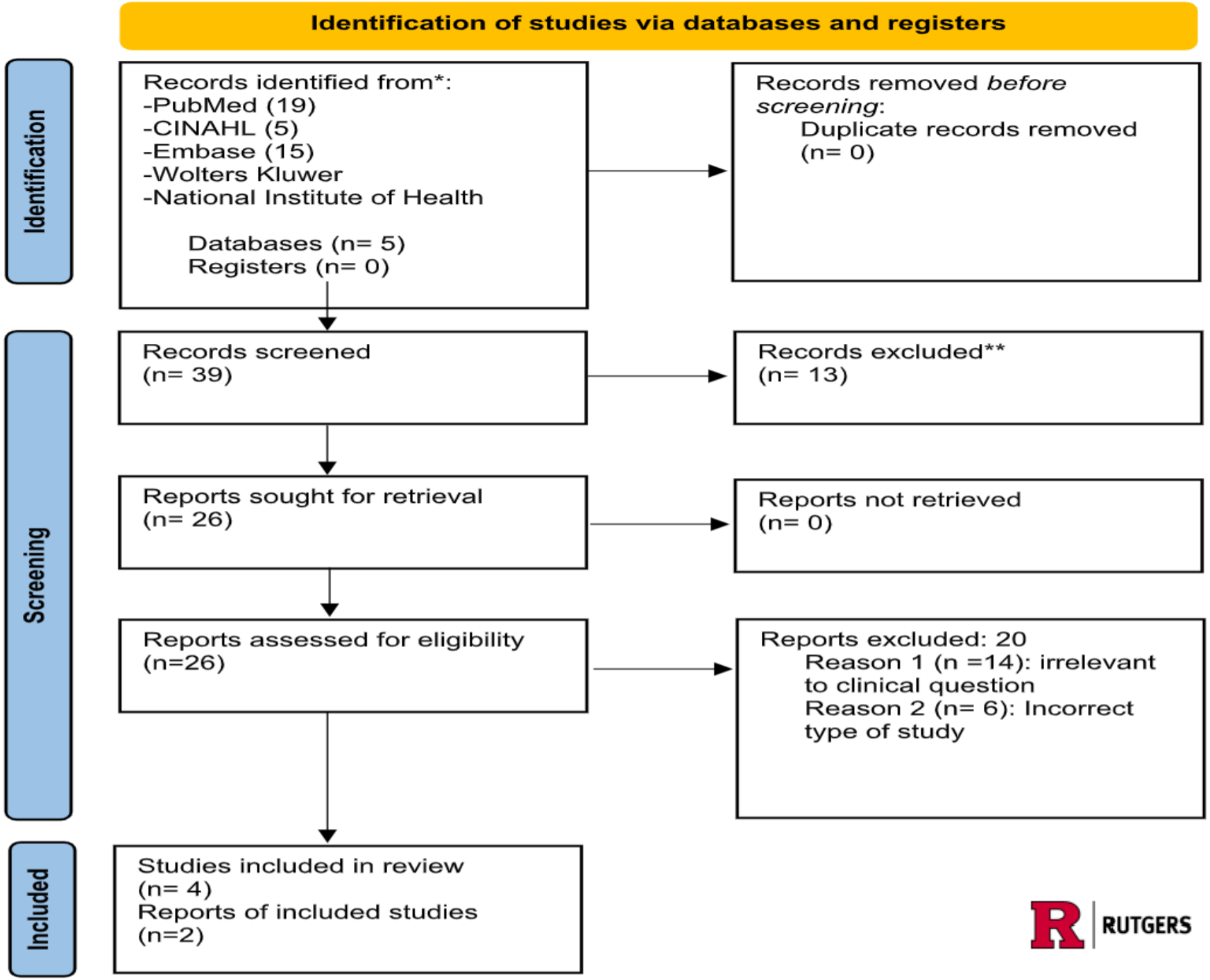
Concept Map to Define Key Search Terms

Concept 1: ***Neuraxial anesthesia*** OR everything in this column	**Concept 2:** ***Neuraxial-route-specific medication administration equipment*** OR everything in this column	**Concept 3:** ***Non-route-specific medication administration equipment*** OR everything in this column
• Epidural • Spinal • CSE - combined spinal epidural • Caudal • Neuraxial • Labor epidural • C-section • Intrathecal • Regional	• NRFit • NRFit connectors • ISO 80369-6 • ISO 80369-6 connectors • Route-specific medication equipment • Mechanically incompatible connection devices • Spinal needles • Epidural needles • Neuraxial catheters • Neuraxial drug delivery systems • Neuraxial anesthesia equipment	• Luer • Luer lock • Non Luer lock • Luer lock syringe • Lock-tip syringe • Luer-slip syringe • Slip syringe • Universal medication administration equipment • Universal drug delivery system • Standard medication administration equipment • Standard drug delivery system • Non-specific drug delivery system • Multi-route medication administration equipment • Multi-route drug delivery system • Catheter connectors

Concept 4: *Medication error* OR everything in this column	Concept 5: *Routes of medication administration* OR everything in this column	Concept 6: *Healthcare costs* OR everything in this column	Concept 7: *Patient safety* OR everything in this column
• Tubing misconnection • Medication administration • Medication dispensing • Adverse drug event • Adverse event • Drug use error • Risk management • Hospital losses • Sentinel event • Wrong-route medication administration • Drug administration mistake • Medication administration mistake • Drug therapy errors • Medical errors	• Intravenous • IV • Catheters • Intraosseous • IO • Enteral (nasogastric tubes, Orogastric tubes, Jejunostomy tubes) • Respiratory (endotracheal tube, tracheostomy) • Subcutaneous • Intramuscular • Neuraxial	• Healthcare expenses • Medical costs	• Patient safety initiatives • Patient harm • Clinical safety • Error prevention • Safety protocols • Safety standards • Safety measures Medication safety • Healthcare quality • Quality improvement

PRISMA Diagram

Preferred
Reporting
Items for
Systematic Reviews &
Meta
Analysis



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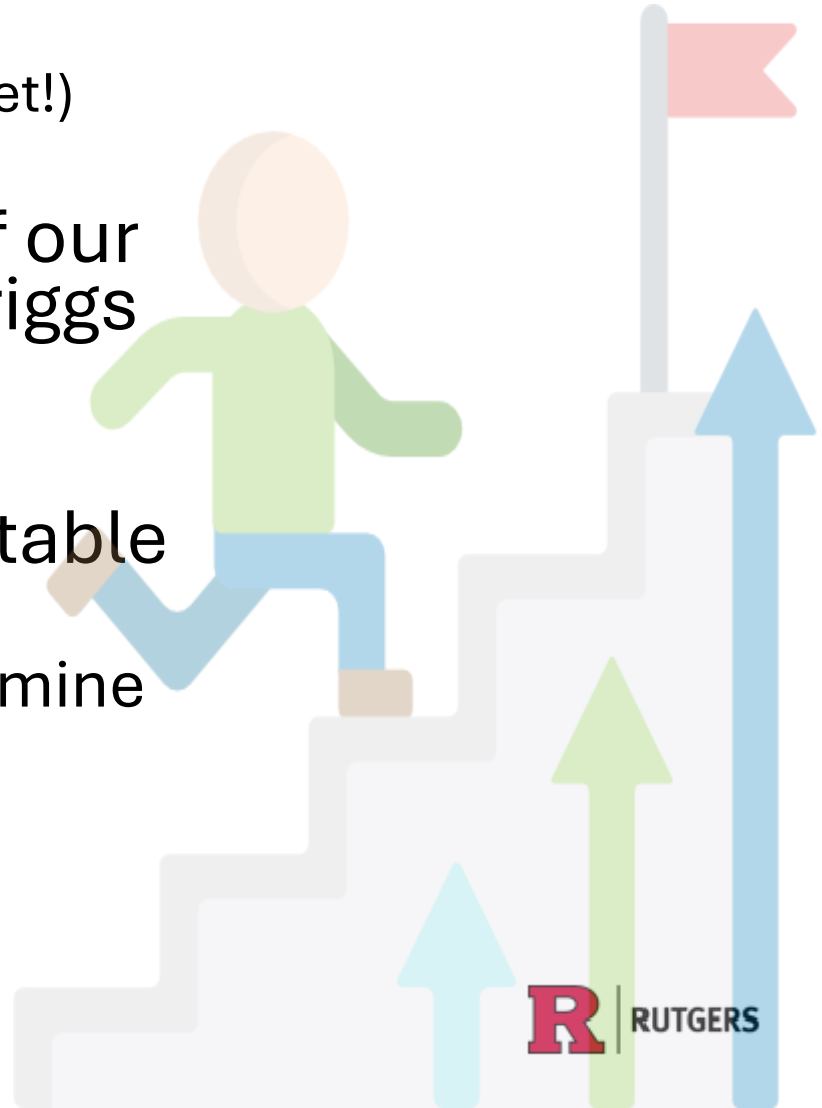
Next Steps & Current phase of systematic review

- Current ongoing tasks: (We are not done with this SR yet!)
  - ***Critical appraisal*** → Determine the quality of our obtained articles with standardized Joanna Briggs Institute (JBI) evaluation tools & checklists.
  - ***Data extraction*** → Extract data and organize table of evidence.
    - Categorize evidence based on strength and determine which articles are appropriate for inclusion in our systematic review and meta-analysis.
  - ***Data Synthesis & Data Analysis***



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Quality Appraisal Strategy: Use JBI critical appraisal tools & ✓lists

Author (Abramyab et al., 2024) Year 2024 Record Number 1

JBI CRITICAL APPRAISAL CHECKLIST FOR SYSTEMATIC REVIEWS AND RESEARCH SYNTHESES		No	Unclear	Not applicable
1. Is the review question clearly and explicitly stated?	☒	☐	☐	☐
2. Were the inclusion criteria appropriate for the review question?	☒	☐	☐	☐
3. Was the search strategy appropriate?	☒	☐	☐	☐
4. Were the sources and resources used to search for studies adequate?	☒	☐	☐	☐
5. Were the criteria for appraising studies appropriate?	☒	☐	☐	☐
6. Was critical appraisal conducted by two or more reviewers independently?	☒	☐	☐	☐
7. Were there methods to minimize errors in data extraction?	☒	☐	☐	☐
8. Were the methods used to combine studies appropriate?	☒	☐	☐	☐
9. Was the likelihood of publication bias assessed?	☒	☐	☐	☐
10. Were recommendations for policy and/or practice supported by the reported data?	☒	☐	☐	☐
11. Were the specific directives for new research appropriate?	☒	☐	☐	☐

Overall appraisal: Include ☒ Exclude ☐ Seek further info ☐

Author Viscusi et al. Year 2020 Record Number 7

JBI CRITICAL APPRAISAL CHECKLIST FOR SYSTEMATIC REVIEWS AND RESEARCH SYNTHESES		No	Unclear	Not applicable
1. Is the review question clearly and explicitly stated?	☒	☐	☐	☐
2. Were the inclusion criteria appropriate for the review question?	☒	☐	☐	☐
3. Was the search strategy appropriate?	☒	☐	☐	☐
4. Were the sources and resources used to search for studies adequate?	☒	☐	☐	☐
5. Were the criteria for appraising studies appropriate?	☐	☐	☒	☐
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8. Were the methods used to combine studies appropriate?	☒	☐	☐	☐
9. Was the likelihood of publication bias assessed?	☐	☒	☐	☐
10. Were recommendations for policy and/or practice supported by the reported data?	☒	☐	☐	☐
11. Were the specific directives for new research appropriate?	☒	☐	☐	☐

Overall appraisal: Include ☒ Exclude ☐ Seek further info ☐

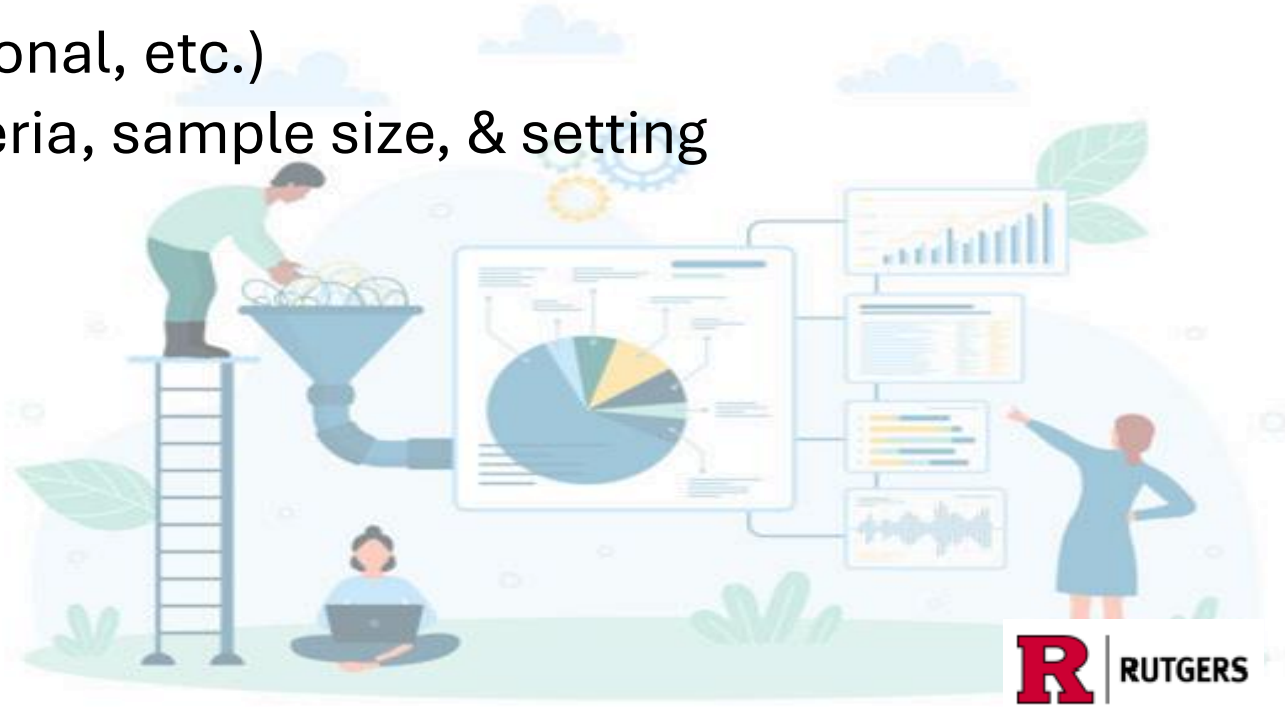
Data Extraction

Meticulous review of each article to ensure:

1. Article answers the central PICO question.
2. Data extracted is pertinent and relevant to review question.

<u>Included data will be entered into a comprehensive ***Table of Evidence:***</u>

- Author, year
- Type of evidence (RCT, cohort, observational, etc.)
- Population, inclusion and exclusion criteria, sample size, & setting
- Description of intervention & control
- Method of statistical analysis
- Limitations
- Findings & outcomes
- Author's conclusions
- JBI appraisal: Level & quality of evidence
- Comments of reviewers



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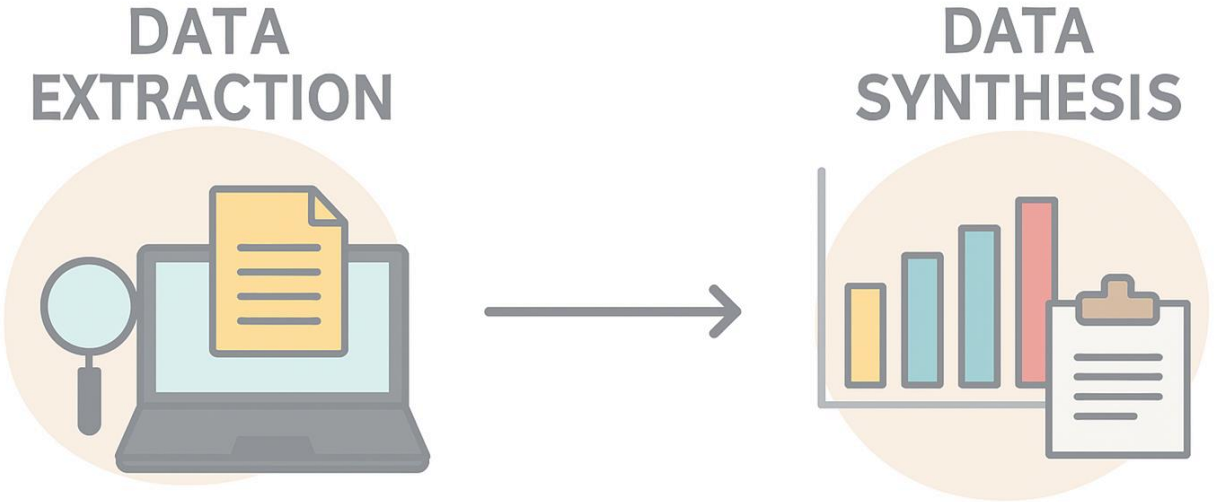
Data Synthesis

- Data synthesis - the process of combining, generating, or transforming extracted data to **create meaningful insights**, **simulate real-world scenarios**, or **enhance datasets for analysis and decision-making**

- We will describe each of the included studies narratively in our systematic review



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Data Analysis

- Quantitative data, whenever possible, will be pooled in a statistical meta-analysis using a random effects model.
- ***Effect sizes:***
  - Categorical data → expressed as an odds ratio or risk ratio.
  - Continuous data → weighted as mean differences.
    - 95% confidence intervals will be calculated for analysis.
    - Heterogeneity: assessed statistically using standard Chi-square.

- If statistical pooling is not feasible, the findings will be analyzed using **Cochrane's SwiM method** presented in the narrative form.
  - Tables and figures will be added to aid data presentation, when appropriate

Assessing Validity

Internal Validity

Are the results trustworthy?

- Validated by *standardized appraisal tools*
  - ↳ JBI checklists
- *Clear inclusion/exclusion criteria* have been defined
  - ↳ Avoids selection ambiguity
- *Standardized data extraction*
  - ↳ Use of a table of evidence with defined data to be extracted

External Validity

Can the results be generalized?

- Transferability – Can the results be applicable to clinical practice in the US, as it is in other developed countries?

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Addressing Bias

Selection Bias:

- Use of *multiple databases* to ensure *all relevant studies* are included.
- Use backward citation chaining to find additional resources from included & appraised articles.

Reviewer Bias:

- Each article appraised must be reviewed by *at least two* team members
- This will *reduce bias* - Researcher determines an article is strong enough to include for review, when in fact, it is not.

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Anticipated Findings

- ISO 80369-6 system is **easy to use** and **clinicians adapt quickly**

- The ISO 80369-6 compliant system can **significantly reduce the risk of misconnections between conventional syringes and spinal needles**, with prior studies reporting **clinician agreement rates as high as 98%**

- Implementation of the system is anticipated to **decrease accidental administration of intravenous medications into the intrathecal or epidural space**, thereby **enhancing patient safety.**

- The system can be **cost-effective:**
  - Same cost as traditional equipment
  - Purchasing an alternative product that is safer and provides equivalent utility to traditional Luer lock devices.
  - Net even balance.
- A **lean business model**:
  - ↓**costs** of future malpractice lawsuits.
  - ↓**costs** from prolonged patient length of stays from experiencing adverse medication event.

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Dissemination of Information & Use of Findings

- *Educate colleagues* on technology
  - Introduce findings to hospital administration throughout our various clinical rotations
  - Introduce findings through presentations at formal conference events – wooh, NJANA!
- Break down & perform a cost-analysis of the potential *cost savings* that hospitals may achieve by *reducing wrong route medication errors*.
- *Decrease stress on clinicians* (especially during stressful situations) thanks to the near impossibility of making a medication error at the point of administration → increases morale ☺.
- *Globalize the United States healthcare syste*m with the rest of the countries in the world (a single new universal standardized system).
- Makes communication & care between countries easier and safer.

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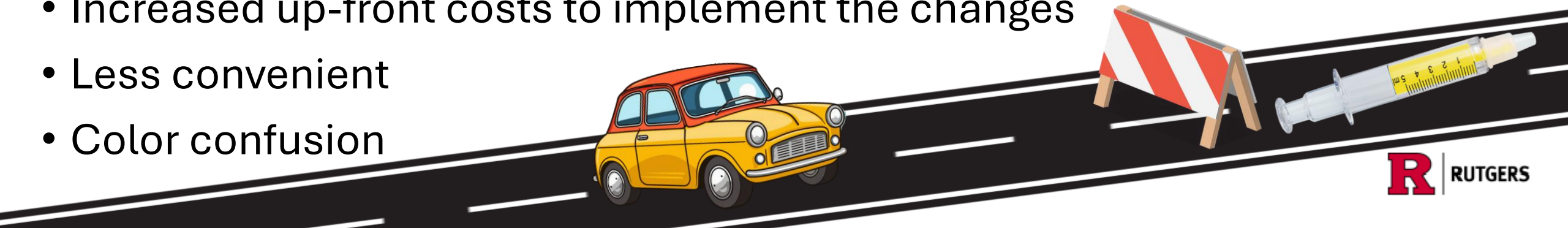
Anticipated Challenges

- Adopting new medical practices can be long and arduous…Introducing policies encouraging new technologies or evidence-based practices can be difficult.
- Resistance to change - Implementing new technology & equipment throughout the entire United States
- Limited research in the United States…dependent on overseas research
- Limited to neuraxial anesthesia (however, consider entire line of ISO 80369 series for route-specific medication administration equipment)
- Increased up-front costs to implement the changes
- Less convenient
- Color confusion



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THANK YOU!

QUESTIONS or COMMENTS