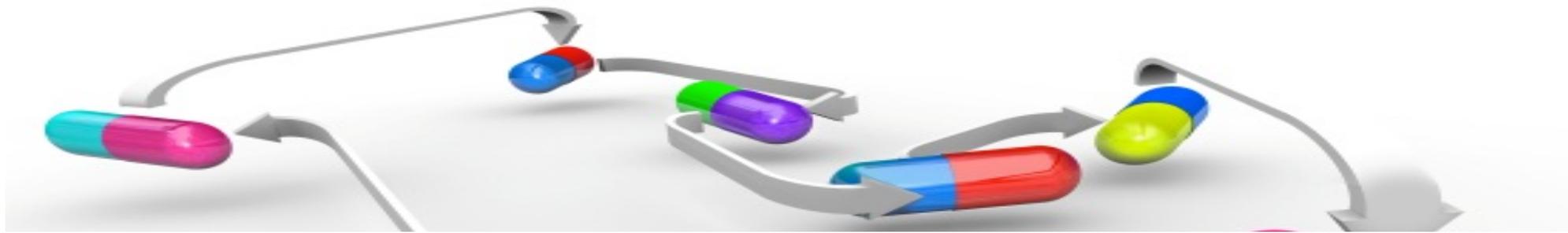




# Outpatient Polypharmacy in Children with Neurodisability and Medical Complexity

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# Presenter Disclosure

- **Presenter:** James Feinstein, MD MPH
- **Relationships with commercial interests:**
  - Grant Support: National Institute of Child Health & Human Development
  - Speakers Bureau/Honoraria: None
  - Consulting Fees: None
  - Other: None

This activity has received funding from the Lucile Packard Foundation for Children's Health.



# Presenter Disclosure

- **Presenter:** Lucas Orth
- **Relationships with commercial interests:**  
No potential conflicts of interest.

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# Accreditation

## Accreditation Statement

This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint providership of Northwestern University Feinberg School of Medicine and University of Toronto/Sick Kids Hospital. The Northwestern University Feinberg School of Medicine is accredited by the ACCME to provide continuing medical education for physicians.

## Credit Designation Statement

The Northwestern University Feinberg School of Medicine designates this live activity for a maximum of 1.0 *AMA PRA Category 1 Credit(s)*<sup>™</sup>. Physicians should claim only the credit commensurate with the extent of their participation in the activity.



# Objectives

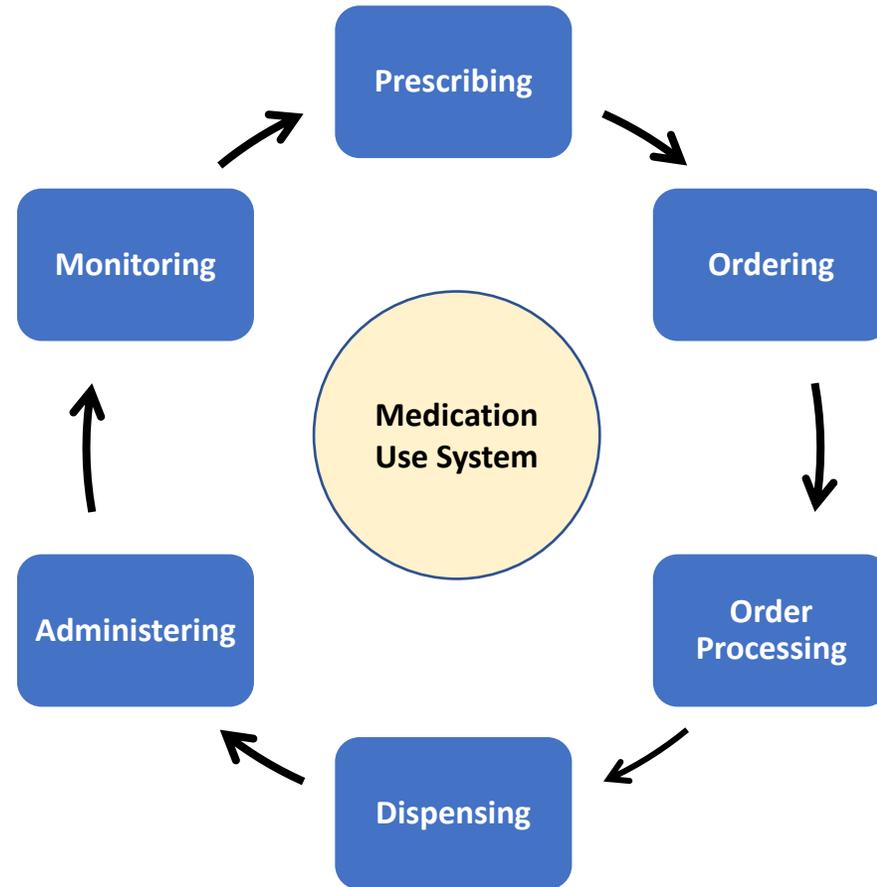
1. Describe polypharmacy in children with neurodisability and medical complexity
2. Recognize the adverse consequences of polypharmacy
3. Demonstrate opportunities to manage & reduce polypharmacy



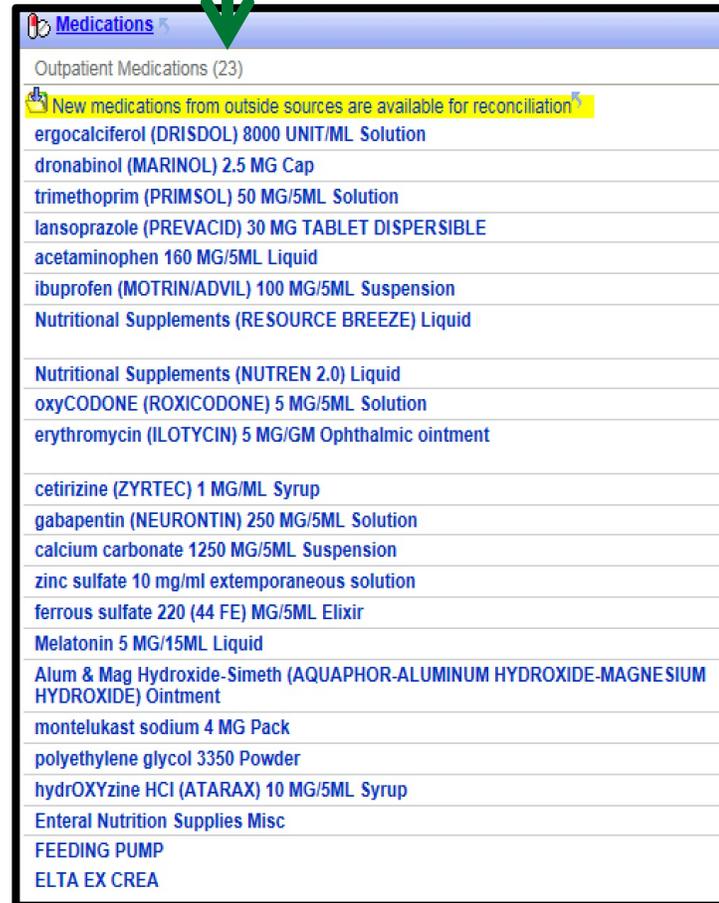
# Some definitions

- Polypharmacy
  - Concurrent use of  $\geq 5$  medications
- Adverse drug event (ADE)
  - Harm due to exposure to a medication
  - May be preventable or unpreventable
- Drug-drug interaction (DDI)
  - A known or theoretical interaction

# Overview of the medication system



# The problem...



Medications
Outpatient Medications (23)
New medications from outside sources are available for reconciliation
ergocalciferol (DRISDOL) 8000 UNIT/ML Solution
dronabinol (MARINOL) 2.5 MG Cap
trimethoprim (PRIMSOL) 50 MG/5ML Solution
lansoprazole (PREVACID) 30 MG TABLET DISPERSIBLE
acetaminophen 160 MG/5ML Liquid
ibuprofen (MOTRIN/ADVIL) 100 MG/5ML Suspension
Nutritional Supplements (RESOURCE BREEZE) Liquid
Nutritional Supplements (NUTREN 2.0) Liquid
oxyCODONE (ROXICODONE) 5 MG/5ML Solution
erythromycin (ILOTYCIN) 5 MG/GM Ophthalmic ointment
cetirizine (ZYRTEC) 1 MG/ML Syrup
gabapentin (NEURONTIN) 250 MG/5ML Solution
calcium carbonate 1250 MG/5ML Suspension
zinc sulfate 10 mg/ml extemporaneous solution
ferrous sulfate 220 (44 FE) MG/5ML Elixir
Melatonin 5 MG/15ML Liquid
Alum & Mag Hydroxide-Simeth (AQUAPHOR-ALUMINUM HYDROXIDE-MAGNESIUM HYDROXIDE) Ointment
montelukast sodium 4 MG Pack
polyethylene glycol 3350 Powder
hydrOXYzine HCl (ATARAX) 10 MG/5ML Syrup
Enteral Nutrition Supplies Misc
FEEDING PUMP
ELTA EX CREA

# The problem...

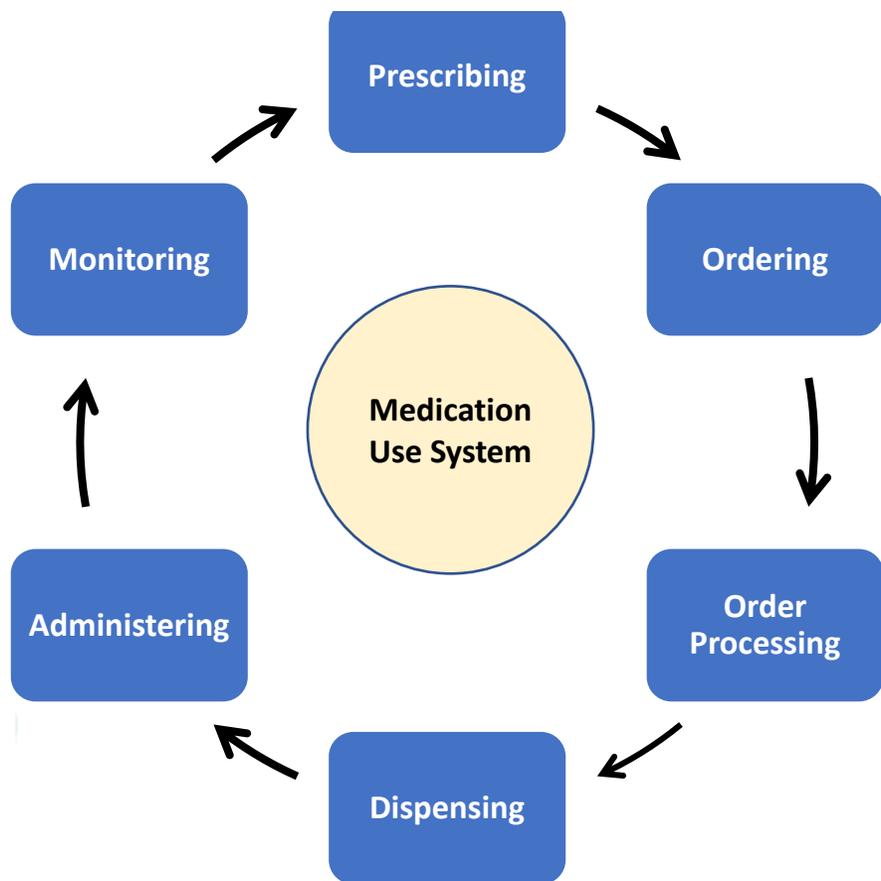
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# Complexity multiplied



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# A few additional complications...

- Lack of high-quality pediatric evidence
  - Limited pediatric dosing, effectiveness, interaction, and side-effect data
  - Extrapolation of adult data
- Few mechanisms to monitor/reduce harm
  - EMR-based solutions
  - Community pharmacists
  - Pharmacists embedded with inpatient teams
- The outpatient setting is truly the Wild West



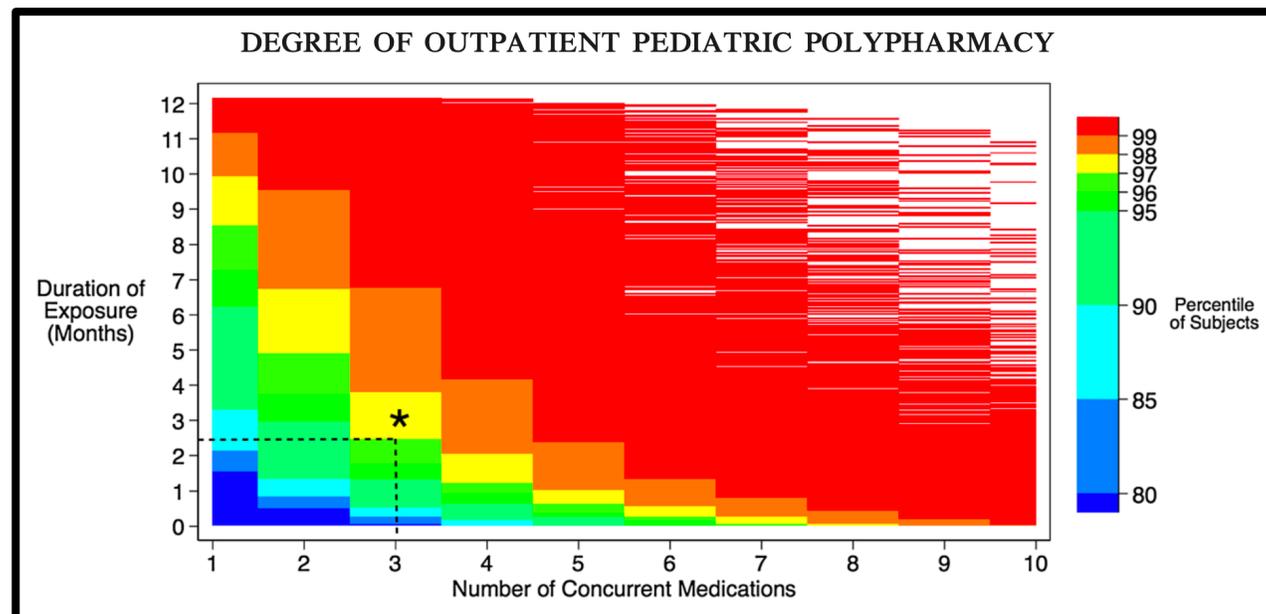


# What do we know?

(Describe polypharmacy in children with neurodisability and medical complexity)

# Who get's polypharmacy?

- Study of annual concurrent polypharmacy
- 242,230 pediatric Colorado Medicaid enrollees
- Risk factors for red areas:
  - Older age
  - Complex chronic conditions
  - Technology dependence





# Polypharmacy is most frequent with NI

- Study of characteristics of complex medication regimens



# Polypharmacy is most frequent with NI

- Study of characteristics of complex medication regimens
- 156 children with medical complexity and polypharmacy

# Polypharmacy is most frequent with NI

- Study of characteristics of complex medication regimens
- 156 children with medical complexity and polypharmacy

**Table 1.** Demographic, Clinical, and Medication-Related Characteristics of Children With Medical Complexity and Complex Medication Regimens (N = 156)

Characteristic	Result
Complex chronic condition, n (%)	156 (100)
Neurological impairment, n (%)	120 (77)
Number of medications in all patients, median (IQR)	8 (5–10)
≥10 Medications	
Patients receiving, %	23.1
Number of medications, median (IQR)	11 (10–13)
≥1 High-risk medication	
Patients receiving, %	95.5
Number of high risk medications, median (IQR)	3 (2–4)
≥1 Compounded medication	
Patients receiving, %	35.9
Number of compounded medications, median (IQR)	1 (1–2)

# Why does polypharmacy occur?

**Co-occurring  
Chronic  
Conditions of the  
Nervous System**

Sensory (26-36%)

Learning (29-33%)

Neurologic (40%)

Mental / Behavioral (61%)

**Co-occurring  
Chronic Conditions  
of Other Body  
Systems**

Endocrine (19%)

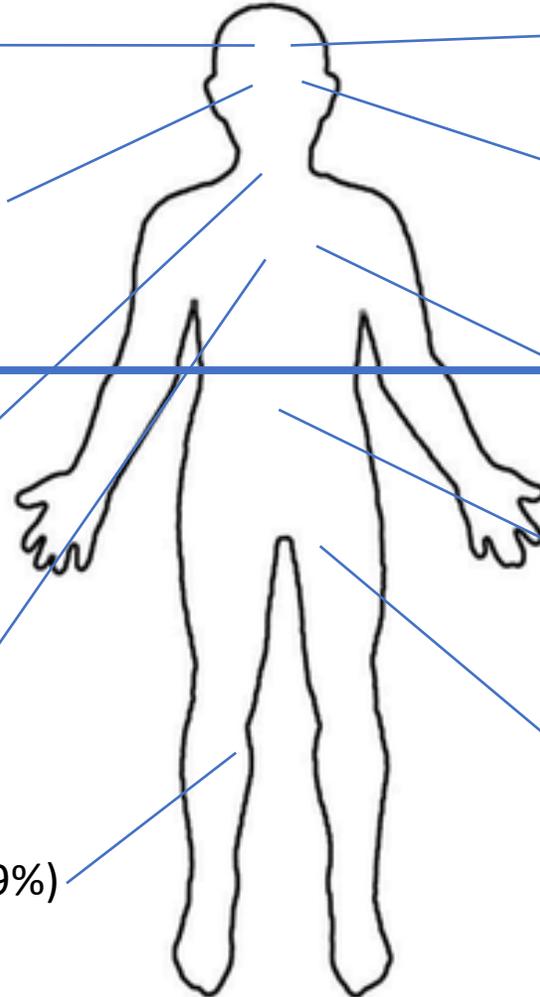
Respiratory (87%)

Musculoskeletal (29%)

Cardiac (32%)

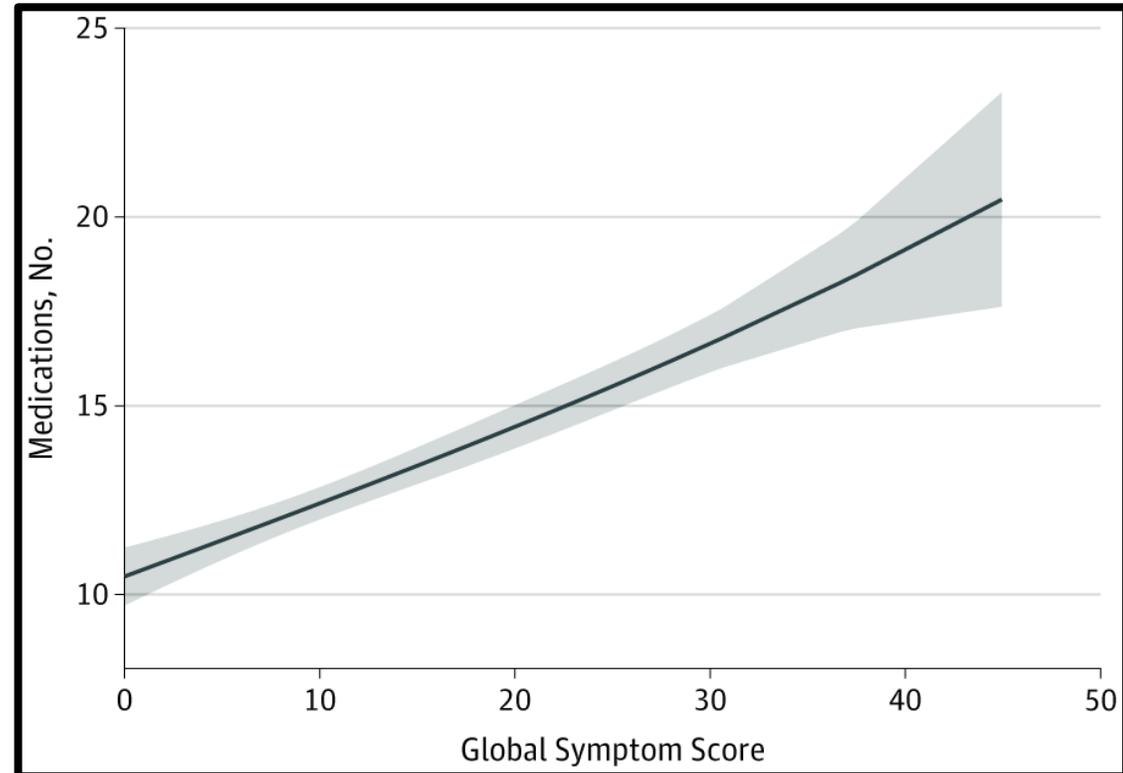
Digestive (49%)

Renal (3%)  
Urologic (16%)



# Why does polypharmacy occur?

- Multiple co-morbidities can result in multiple symptoms
- Study of symptoms in 100 children with SNI
- Higher symptom burdens are associated with polypharmacy

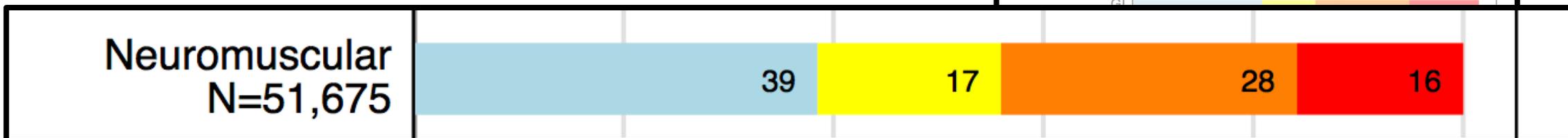
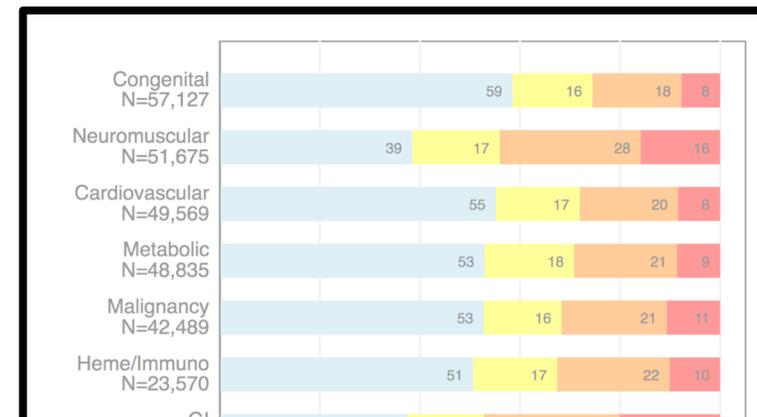


# When/where does it occur?

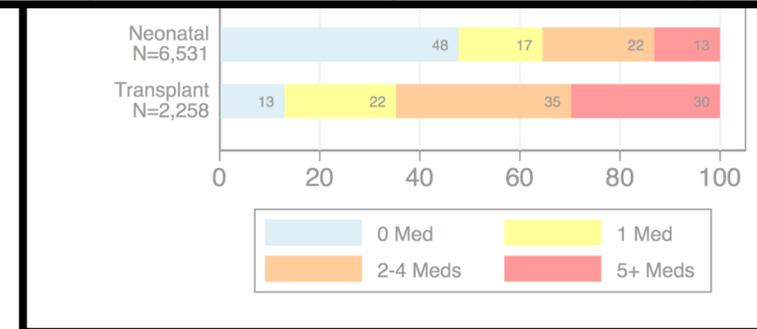
Health Care Service Category	Use During Each Year of Life (Proportion Who Used Each Service, %)					Trend Analysis OR (95% CI)
	1	2	3	4	5	
Inpatient	66.8	12.9	8.9	7.0	5.8	0.35 (0.34 to 0.36)
ED	67.8	62.8	55.2	49.1	44.4	0.78 (0.77 to 0.79)
Outpatient						
Primary care	97.7	95.2	91.2	87.8	88.7	0.69 (0.68 to 0.71)
Specialty care	84.8	78.1	71.2	64.4	69.0	0.79 (0.78 to 0.80)
Therapy	50.7	44.3	37.5	33.8	32.1	0.82 (0.81 to 0.83)
Mental health services	25.1	27.1	29.8	26.4	28.0	1.03 (1.01 to 1.04)
Home health	22.3	3.8	2.2	2.1	1.9	0.41 (0.39 to 0.42)
Outpatient medications	95.5	92.7	87.7	84.9	84.5	0.73 (0.72 to 0.74)

# What kind of polypharmacy?

- Examined chronic medication use in children with medical complexity
- Chronic medication: 1 fill + 2 refills

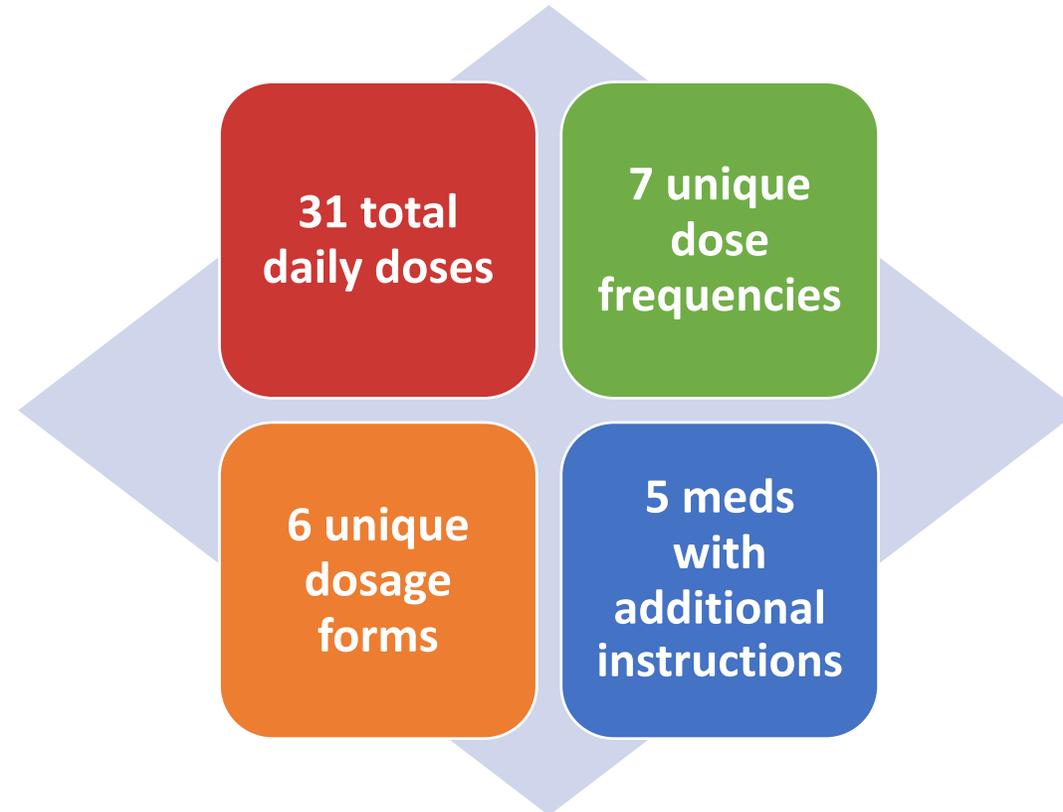


- >60% used chronic medications
- >44% used multiple chronic meds



# What kind of polypharmacy?

- Per patient medication regimen complexity
- 123 children with severe neurological impairment
- Median counts





# What are the problems?

(Recognize the adverse consequences of polypharmacy)

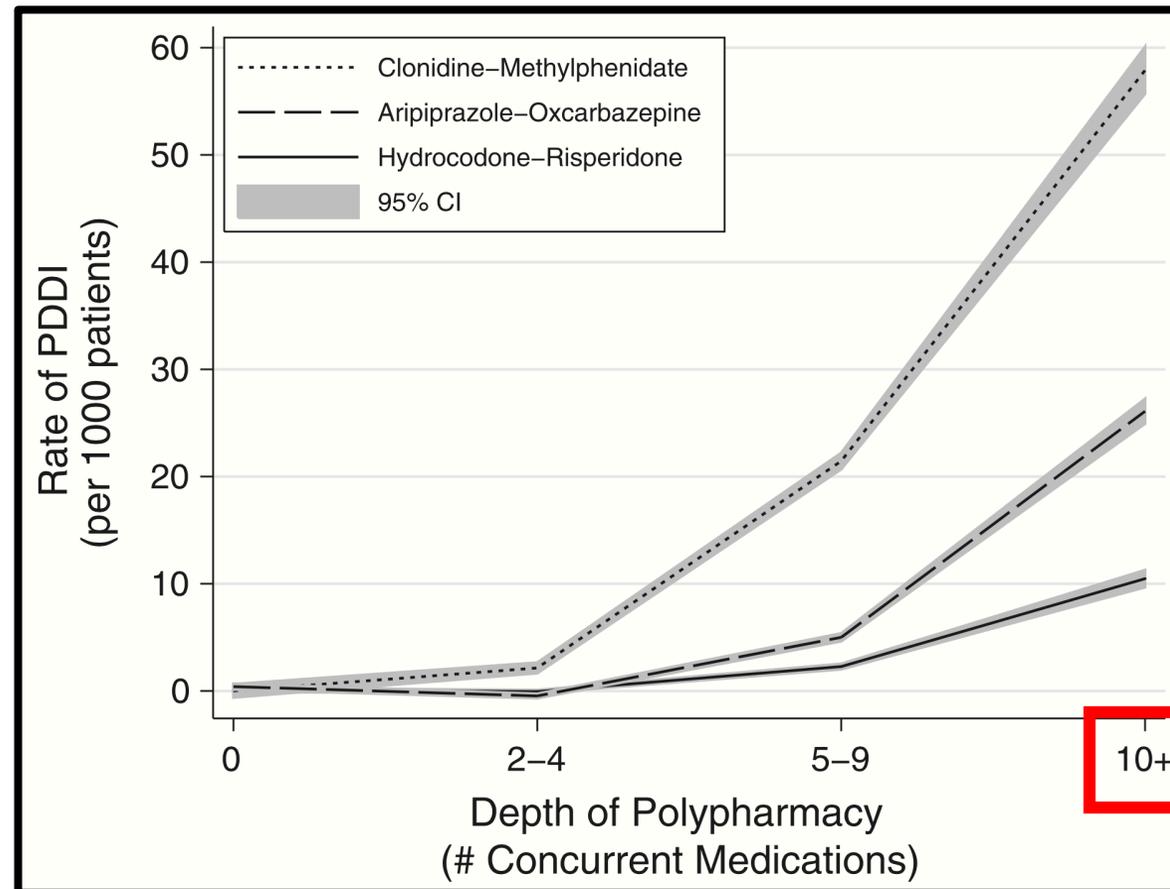
# ADEs and emergency care...

- 144 million ED visits by children 0-18 years old
- 0.5% of all visits associated with ADE
- Children with CCCs had a 5x higher risk of ED visits related to ADEs, compared with other children
- Implicated drugs with the highest rates of ADEs:
  - Psychotropic drugs
  - Anti-microbial drugs
  - Anticonvulsants
  - Hormones/steroids
  - Analgesics



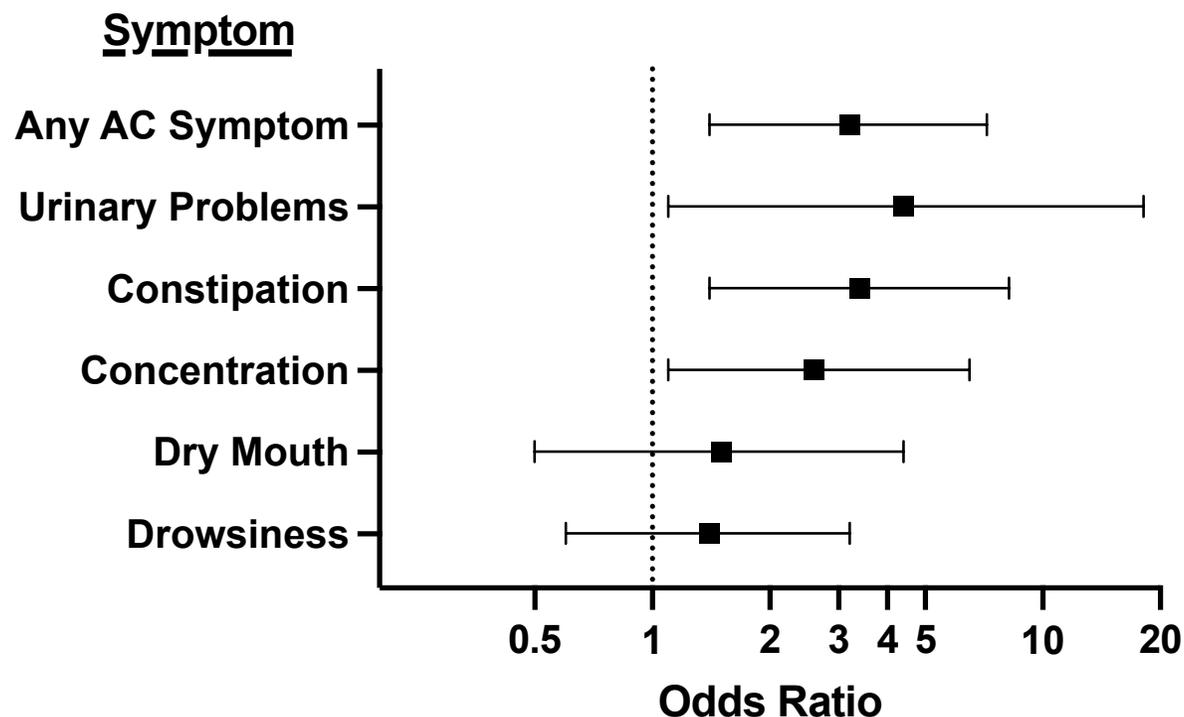
# DDIs are prevalent in polypharmacy...

- Colorado Medicaid study
- 3 tracer drug interactions
- Rates of DDI increased with increasing levels of polypharmacy



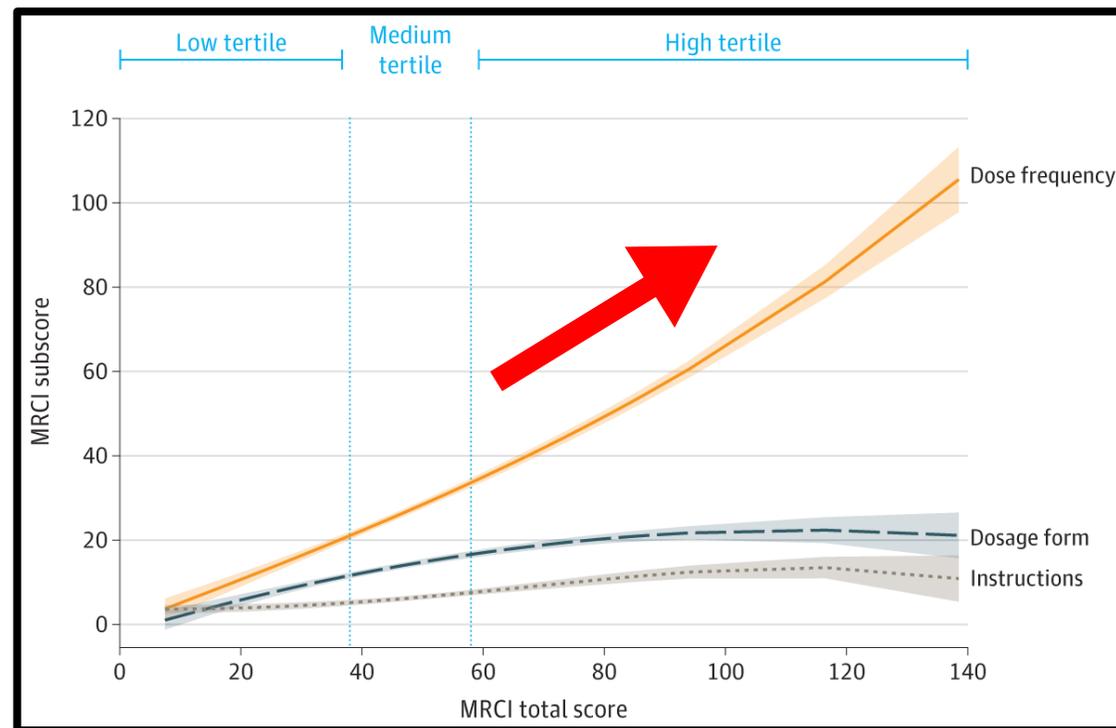
# DDI have potential consequences...

- 123 children with SNI
- Total anticholinergic burden measured using Anticholinergic Cognitive Burden score
- Parent-reported anticholinergic symptoms assessed



# Polypharmacy → caregiver burden

- Home medication regimen complexity assessed using medication regimen complexity index (MRCI) scores
- 123 patients with SNI had a median per patient:
  - 31 total daily doses
  - 7 unique dose frequencies
  - 6 unique dosage forms
  - 5 specialized instructions



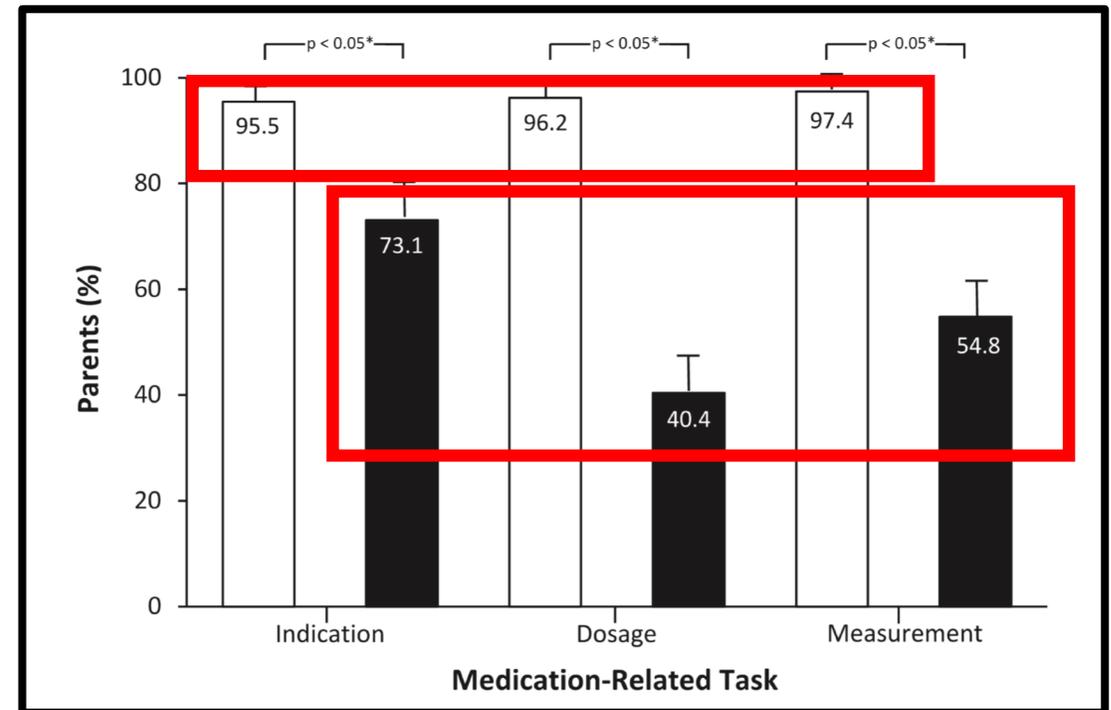


# Unique patients = unique medications

- Compounded medications
  - Allow greater flexibility and ease of administration, but at greater risk (unlimited variability)
- Liquid doses
  - Opportunity for calculation errors
  - Require high level of understanding related to drug concentration
- G-tube/J-tube administration
  - Often rely upon crushed tablets or opened capsules
  - Can introduce overlooked difficulties related to absorption site
- Vitamin and supplements
  - Common, but widely variable and lacking regulatory oversight

# ...But we don't prepare parents enough

- Parents report high confidence in ability to recall medication details and prepare doses appropriately (>90%)
- Demonstrated ability was lower:
  - 73% -- Able to identify the medications used for 2 selected indications
  - 40% -- Able to recall complete dosing parameters for 1 selected high-risk medication
  - 55% -- Able to correctly measure 2 requested liquid medication volumes
- Reinforces need for improved education, particularly when polypharmacy is present

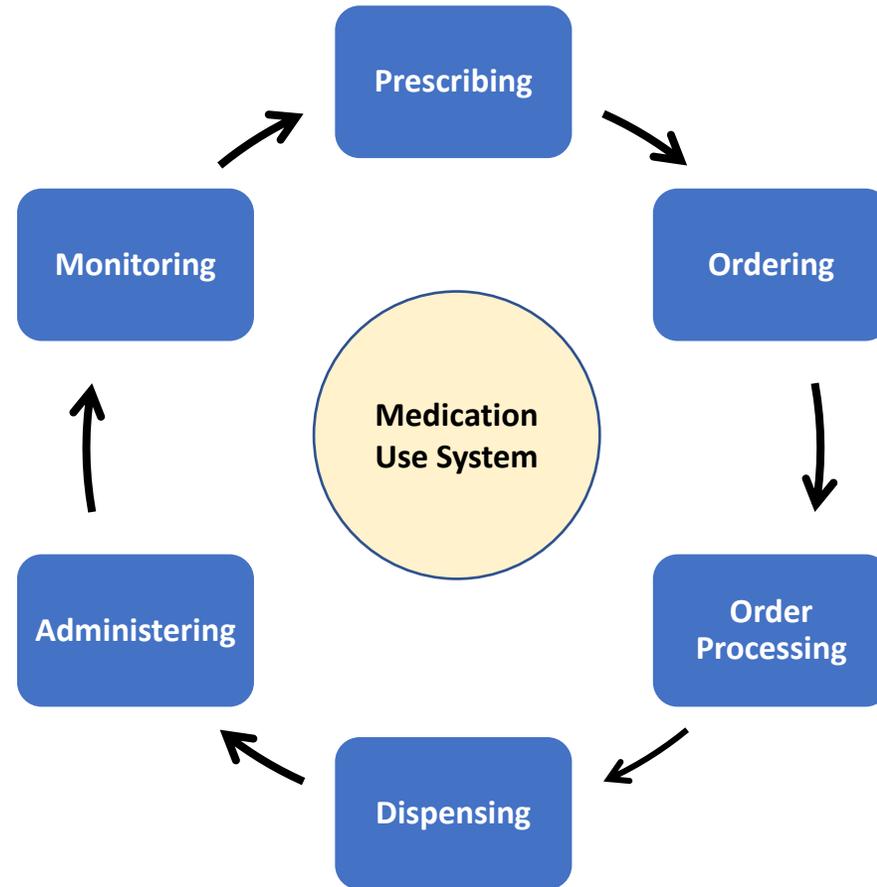




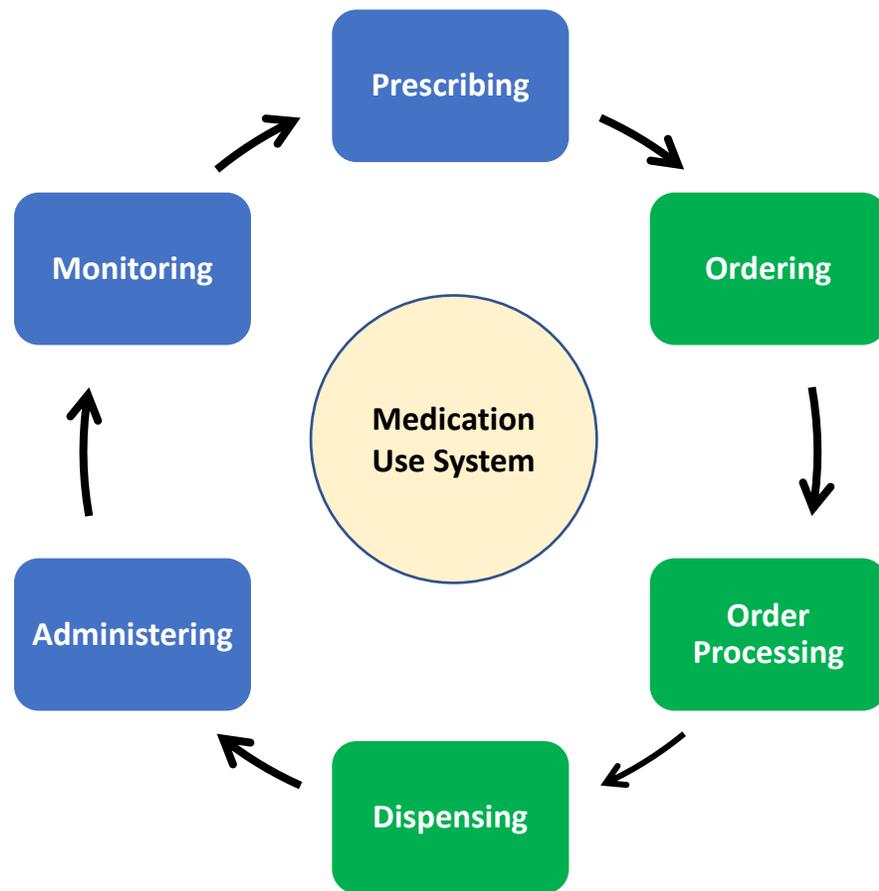
# What can we do?

(Demonstrate opportunities to manage and reduce polypharmacy)

# Overview of the medication system

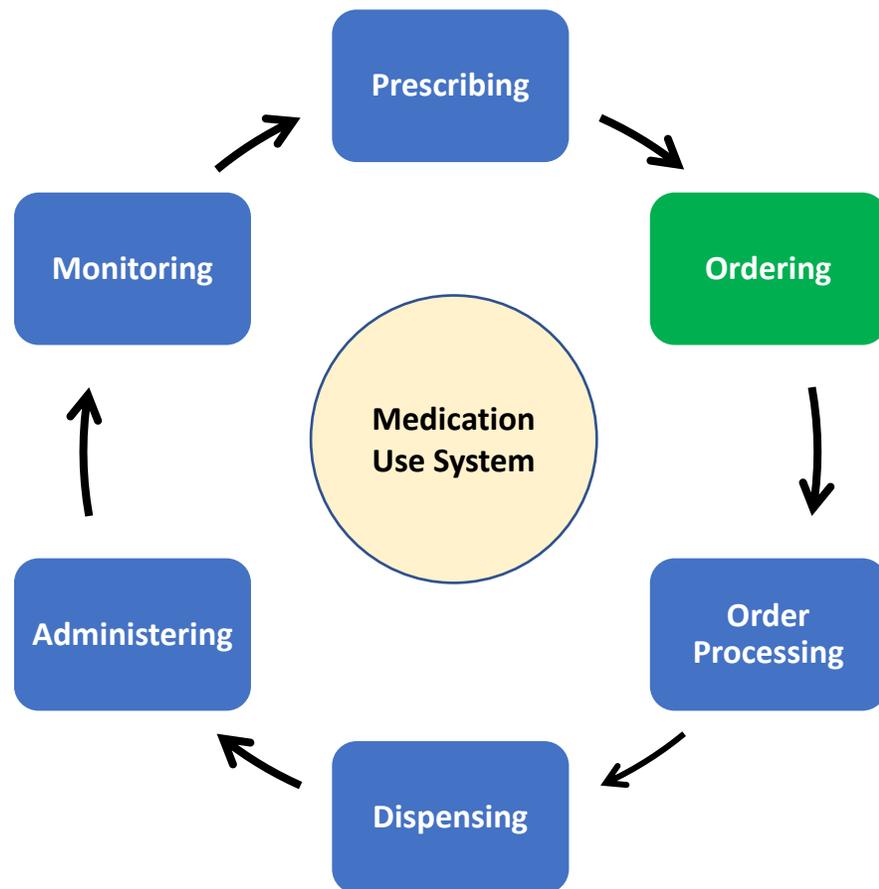


# Focus areas of prior interventions



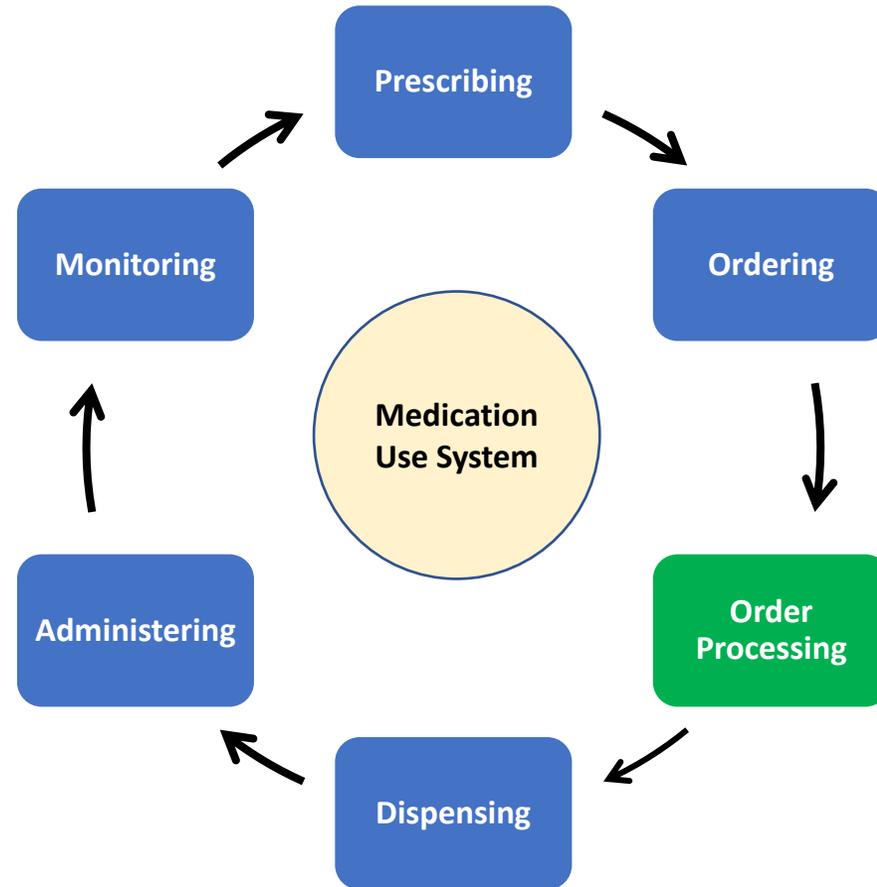
Green areas may be easier to address and where we have placed our efforts to date

# Focus areas of prior interventions



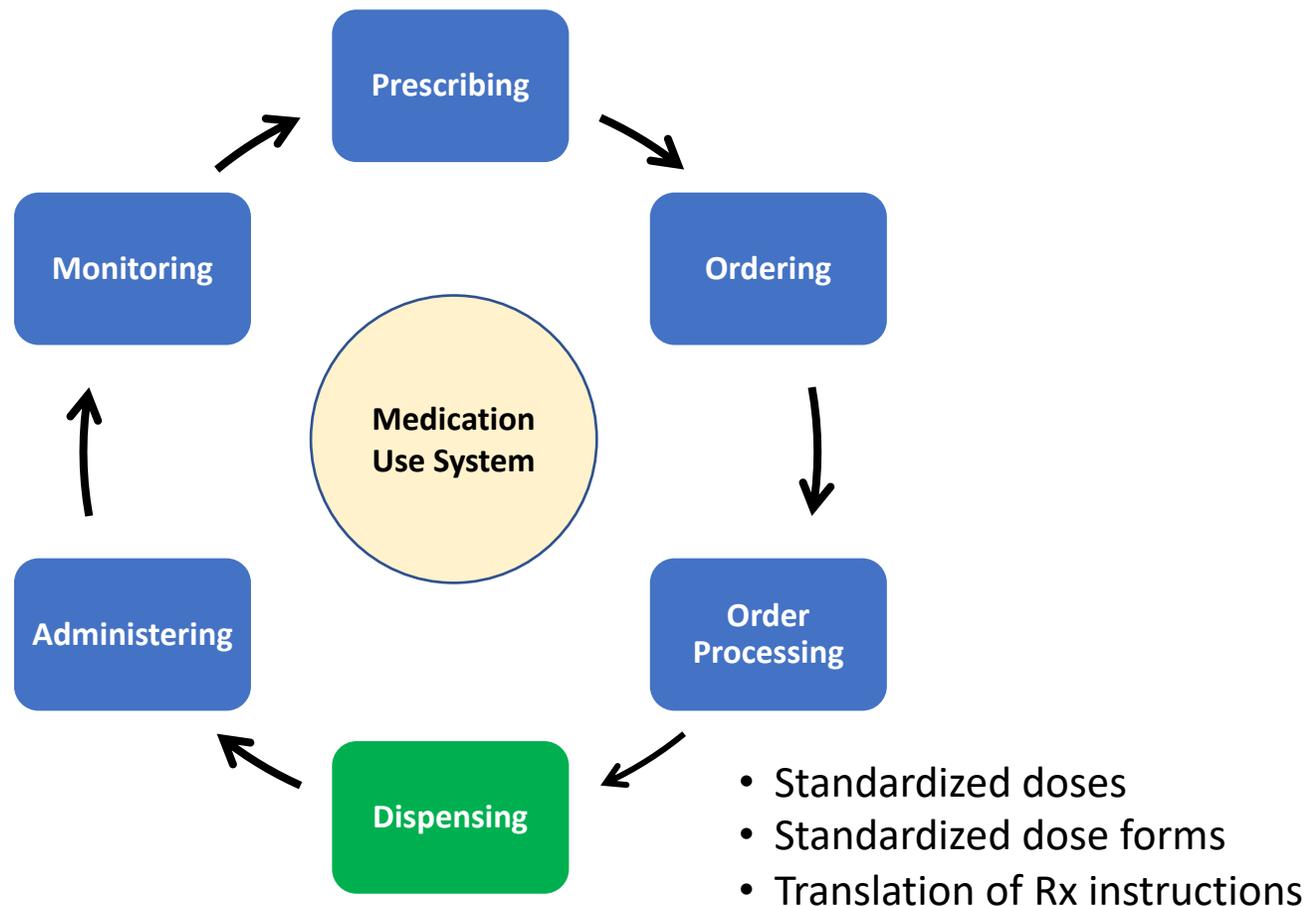
- Computerized provider order entry
- Linked formulary information
- Weight-based dose checking
- Interaction checking

# Focus areas of prior interventions

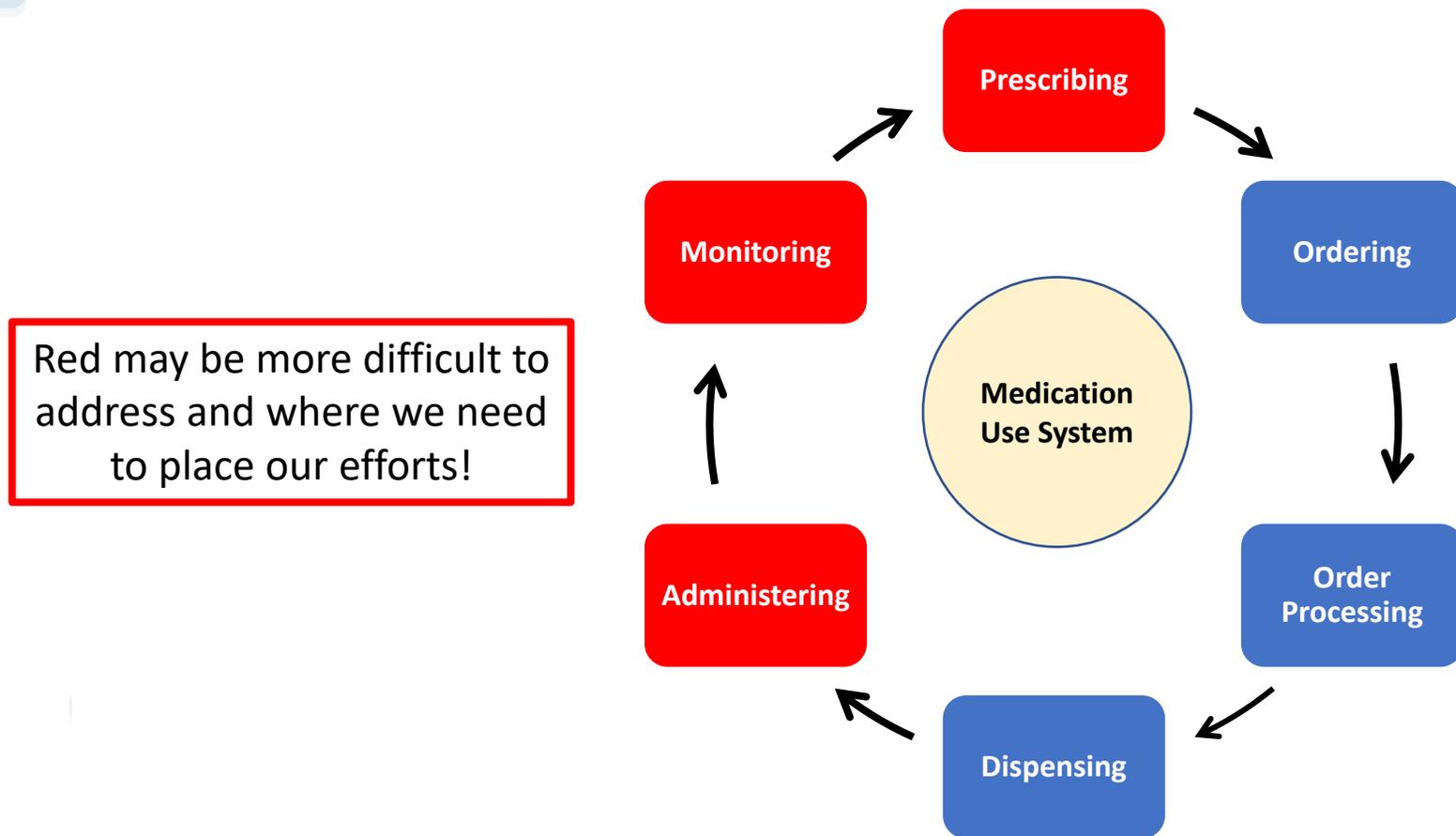


- E-Prescribing

# Focus areas of prior interventions

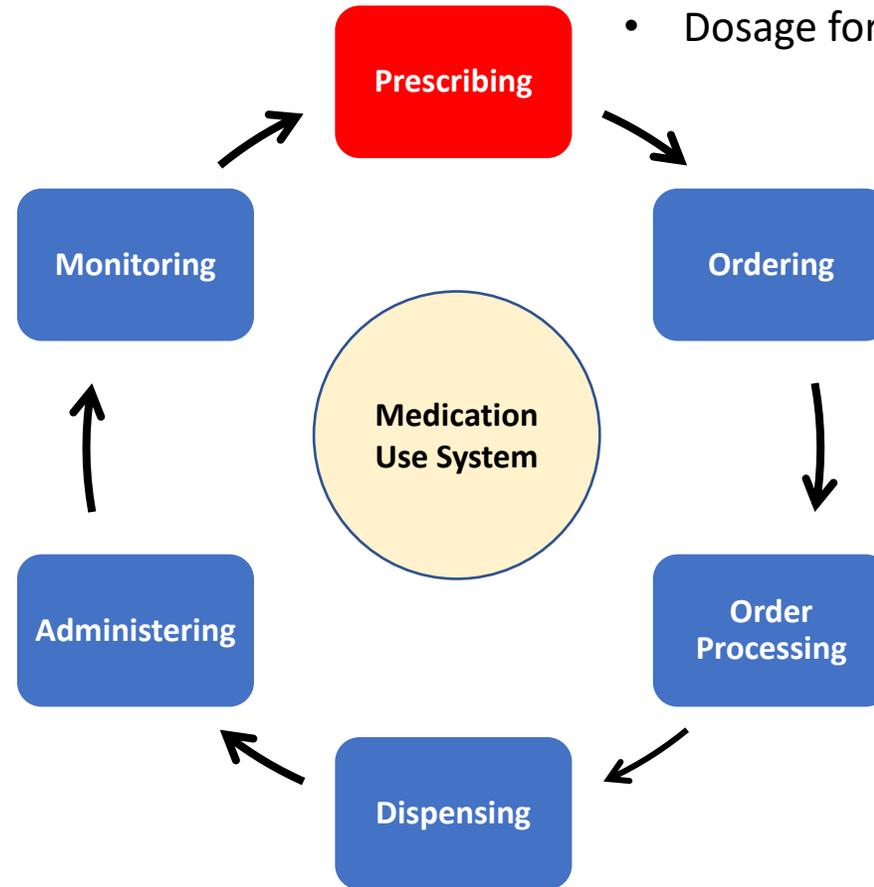


# Focus areas requiring intervention



# Challenges exist

- Majority of medications are used off-label
- Proper medication selection given polypharmacy
- Unique disease-state considerations
- Dosage form considerations



# Improving prescribing

- Can we do a better job generating data to inform prescribing?

**Pharmacokinetics of Understudied Drugs  
Administered to Children Per Standard of Care**

NIH U.S. National Library of Medicine  
*ClinicalTrials.gov*

- Studying drugs used currently and commonly (off-label) in various pediatric age groups, for example:
  - Gabapentin
  - Guanfacine
  - Clobazam
  - Metformin
  - Dexmedetomidine
  - Fosfomycin
  - Oxycodone
  - Risperidone
  - Zolpidem
- Safety & efficacy in rare populations is even more challenging post-marketing



# Improving prescribing

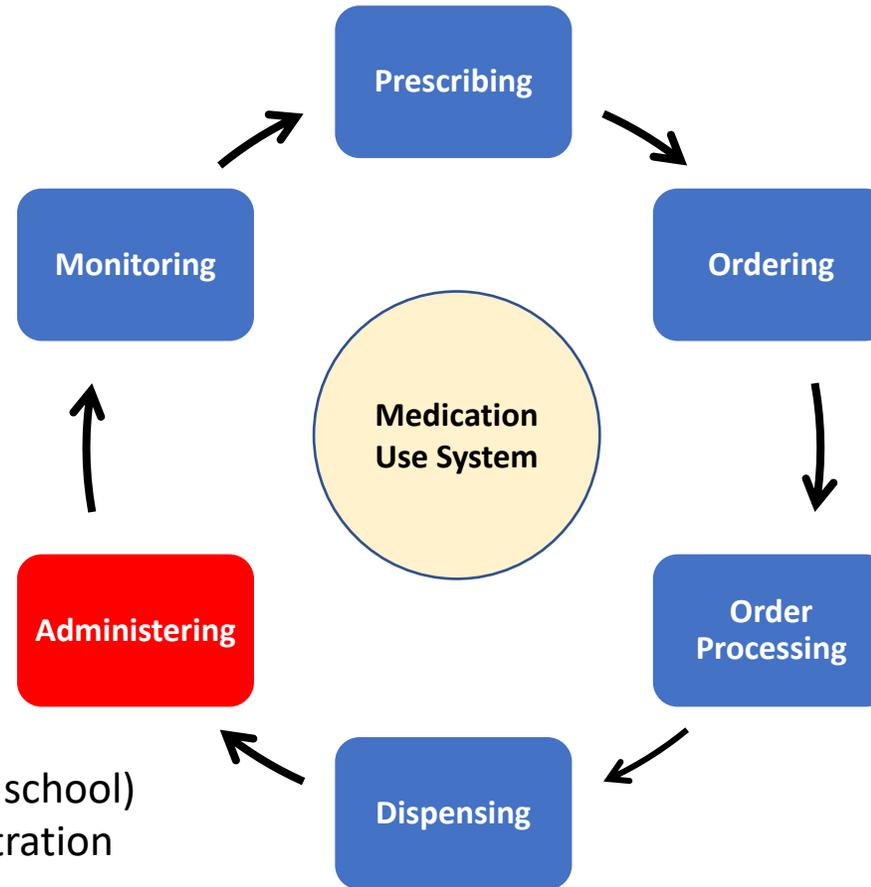
Reviews of Therapeutics |  Full Access

Management of Self-injurious Behaviors in Children with Neurodevelopmental Disorders: A Pharmacotherapy Overview

Management of Sleep Disorders in Children With Neurodevelopmental Disorders: A Review

“Additional data from well-designed studies are desperately needed to gain a better understanding of this common and troublesome problem...  
**Until then, clinicians must rely on the limited available data, clinical expertise, and ongoing systematic monitoring when managing [XYZ] in children”**

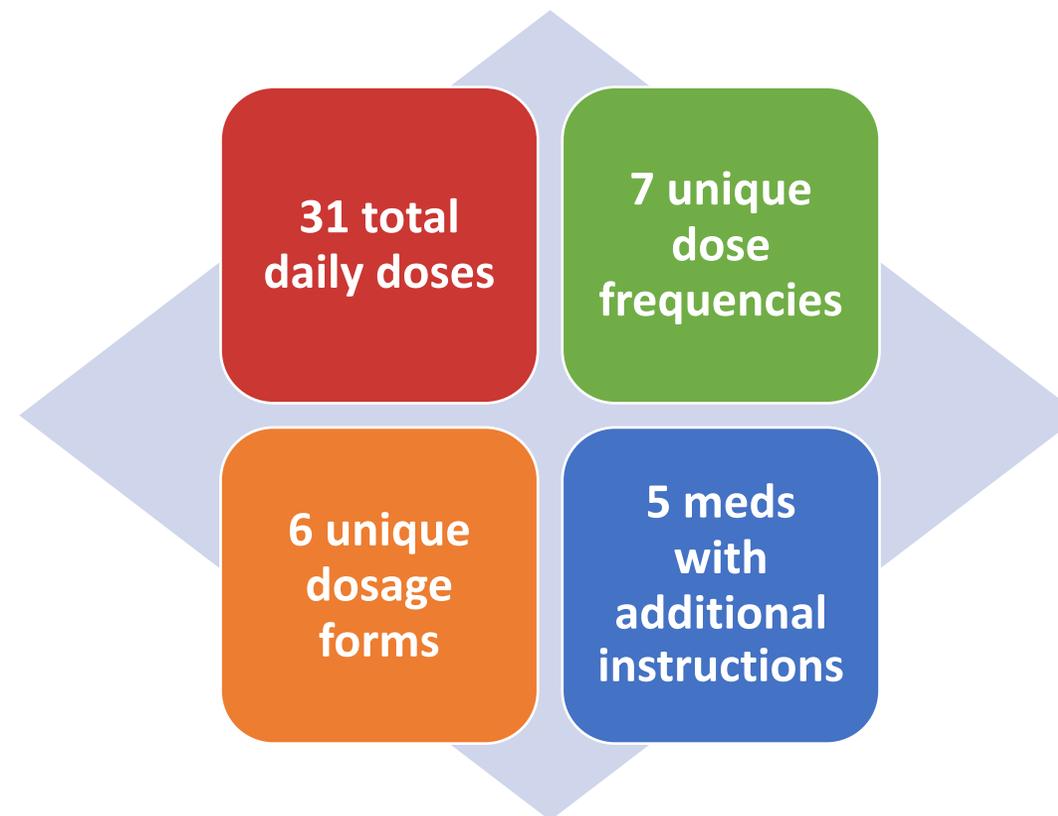
# Challenges exist



- Variable parent/caregiver knowledge/skill related to medication administration
- Administration occurs across multiple settings (e.g., home, school)
- Alternative routes of administration
- Palatability issues

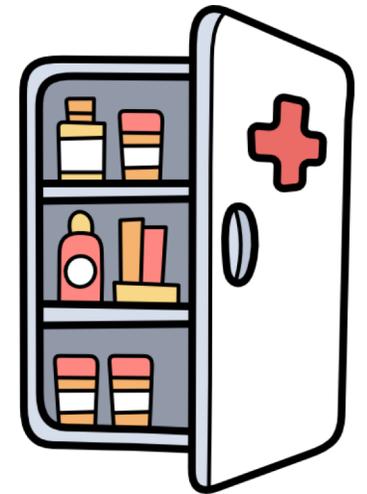
# Improving home administration

- Most importantly, the parent is the home “parent pharmacist” and we need to enhance our ability to support parents



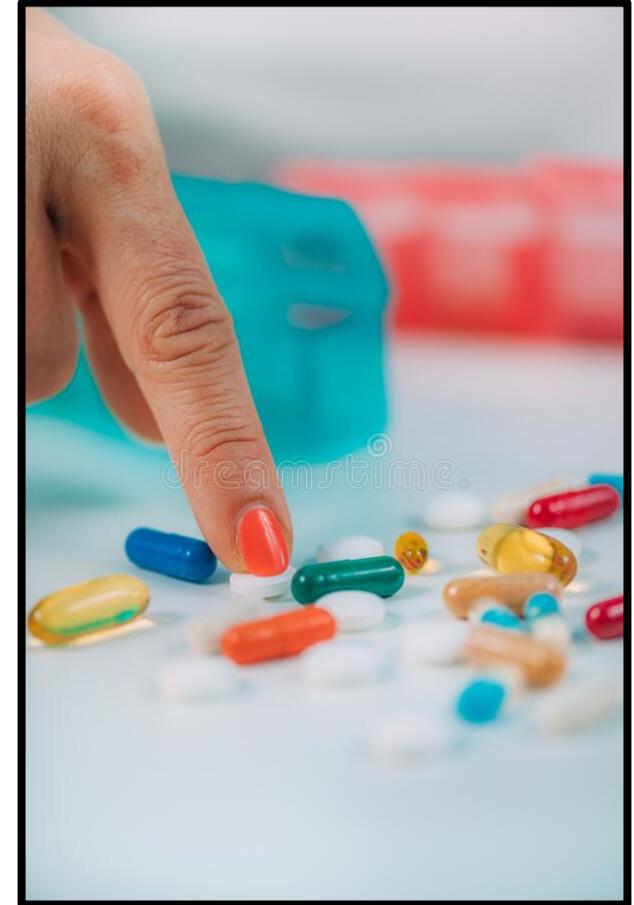
# Supporting “parent pharmacists”

- Reducing medication regimen complexity
  - Simplification of current regimen
  - Targeted attempts to utilize opportunities for “de-prescribing”
- Better job providing tailored advice and instructions
- MTM sessions to proactively monitor for potential issues
- Consistent point of contact
- Mobile technology



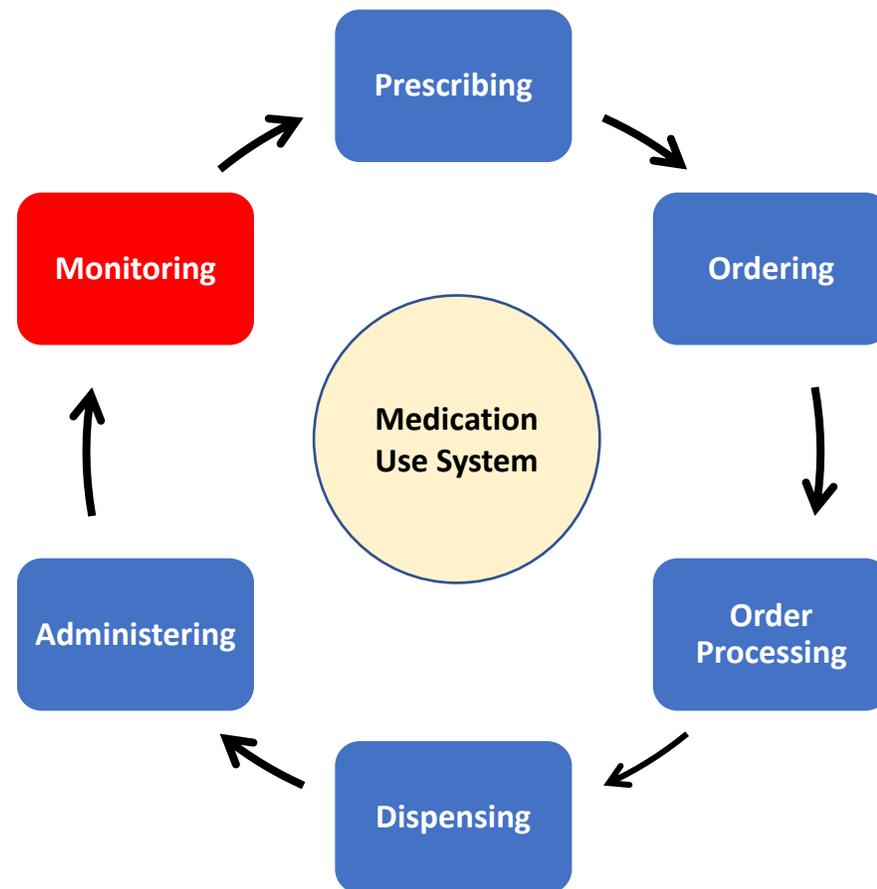
# Pharmacist intervention...

- Planning a randomized controlled trial
- Intervention group will receive pharmacist-based intervention
- Control group will receive usual care
- Major outcomes:
  - Medication complexity
  - Patient symptoms



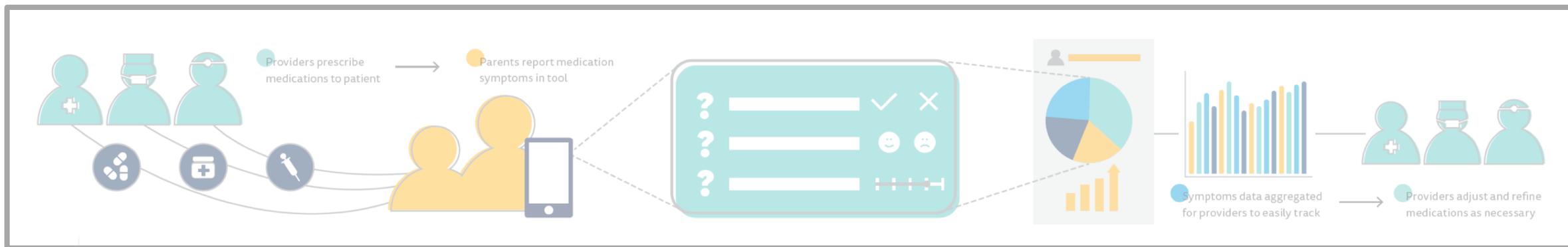
# Challenges exist

- Monitoring of effects occurs by parent/caregiver
- Provider may be unaware until ADE occurs or child presents to healthcare setting
- Difficult to monitor polypharmacy



# Improving monitoring...

- Ongoing study to look at whether changes in symptoms can be detected after medication changes
- Online structured longitudinal symptom reports



- Can be applied to any other intervention to assess patient-level symptom trajectories

# Putting it all together

- Older children with CCCs, particularly NI, at risk of prolonged polypharmacy
- Polypharmacy has real and measurable downstream safety implications
- We have opportunities to improve prescribing, support caregivers in home administration, and enhance monitoring



# Where does this leave us?

- Abundant opportunities to bring together various members of care team to improve medication safety
- The more we can measure needs, responses to interventions, and desired/adverse events, the better we can support patients and parents
- Development of polypharmacy-mitigating strategies is a fun future area to be involved as we think about using technology to harmonize across care domains





# Thank you!

Questions? Ideas? Comments?

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