Pharmacy Residency Research Showcase

Moderated by Elizabeth Monson, PharmD, BCPS

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Objectives

- Identify key components of at least two distinct pharmacy residency research projects presented during the showcase, highlighting research objectives, methodologies, and outcomes.
- Summarize the main findings and practical applications of one specific residency research project, demonstrating the ability to distill complex information into concise and understandable insights.
- Apply critical evaluation skills to assess the appropriateness of research methodologies employed in a presented project, identifying strengths and potential limitations.
- Analyze the impact of residency research on patient care by identifying specific instances where research findings have influenced clinical practices and improved healthcare outcomes.

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Objectives

- Synthesize information from multiple research presentations to propose potential collaborative initiatives of further research directions that could advance pharmacy practice.
- Evaluate the relevance and significance of a presented research project in the context of current healthcare challenges, recognizing its potential to address gaps in knowledge or practice.
- Demonstrate an understanding of at least one research skill or methodology presented in the showcase by outlining how it could be applied to investigate a relevant pharmacy practice issue.
- Engage in collaborative discussions with at least two presenters or attendees, exploring potential opportunities for collaborative research or knowledge-sharing within the pharmacy community.

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Disclosures

- I have no financial interest to disclose

Logistics

- You will hear from 8 pharmacist about their research project, 4 in session 1 and 4 in session 2.
- Each presenter will have 12 minutes for presentation and 3 minutes for questions.
- There will be a short (15 minute) break after session 1 for refreshments.
- Session 2 begins at 3:00 pm in this same room.
- **Must attend both sessions in order to receive CE credit.**

Session 1

- Evaluation of a Pharmacist-led Erythropoietin Stimulating Agent Standard Work Protocol in the Hospital Setting; Alexa Brown, PharmD
- Examining the impact of a pharmacist-managed diabetes care program in an internal medicine clinic:
  A retrospective matched cohort study; Fatme Younes, PharmD
- A Retrospective Comparison of Opioid Medication Choice for the Treatment of Neonatal Iatrogenic Withdrawal; Morgan Schrage, PharmD
- Glucagon-Like Peptide 1 Agonist Impact on Inflammatory Bowel Disease; Rebecca Aubart,PharmD

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Evaluation of a Pharmacist-led Erythropoietin Stimulating Agent Standard Work Protocol in the Hospital Setting

Alexa J Brown, PharmD

PGY1 Pharmacy Resident

Essentia Health Fargo

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Disclosures

- Authors of this presentation have nothing to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation

Objectives

- Purpose:
  - To evaluate the effect of a pharmacist-led ESA standard work policy on appropriate prescribing and dosing among adult patients in the hospital setting
- Specific aims:
  - Identify if a pharmacist-led ESA standard work policy increases the rates of appropriate prescribing including dosing and indication
  - Evaluate if a pharmacist-led ESA standard work policy results in cost savings for the hospital

Background

- Erythropoiesis Stimulating Agents
  - Epoetin alfa
  - Darbepoetin alfa
  - Methoxy-polyethylene glycol-epoetin beta
- Mechanism of Action
  - Mimic the human protein erythropoietin to stimulate red blood cell production from bone marrow
- Main Indications
  - Anemia of CKD
  - Chemotherapy induced anemia

Background

- BLACK BOX WARNING
  - Increased risk of death, myocardial infarction, stroke, venous thromboembolism, thrombosis of vascular access, and tumor progression or recurrence
- Given the extensive literature endorsing the benefits and revealing the risks of ESA use, it is important to exercise optimal and appropriate use to maximize the risk-benefit ratio
- Use of lowest dose sufficient to reduce the need for red blood cell transfusion is essential

Methods

- Design: Case-Control
- Location: Essentia Health-Fargo
- Study Period:
  - Control: January 1, 2023 to June 30, 2023
  - Case: August 1, 2023 to January 31, 2024
- Statistical Analysis
  - Generalized linear mixed models
  - Binary logistic model, with OR (95% CI) and p-value
    - Adjustment for within subject correlations

Population

Inclusion Criteria

- ≥18 years of age
- Received at least one dose of any ESA during the study period while hospitalized

Exclusion Criteria

- Patients being treated for HIV with zidovudine
- If ESA use was to reduce number of blood transfusions during and after major surgeries
- Chronic hepatitis C
- Patients requiring ESA use due to refusing blood transfusions

Definitions

Appropriate ESA prescribing

- The prescribing was considered appropriate if the patient's clinical picture aligned with the indications within the standard work policy

Appropriate ESA dosing

- The dosing was considered appropriate if the patient's clinical picture aligned with the dosing recommendation within the standard work policy

*The standard work aligns with current prescribing and dosing guidelines from the FDA, KDIGO, and NCCN

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Standard Work

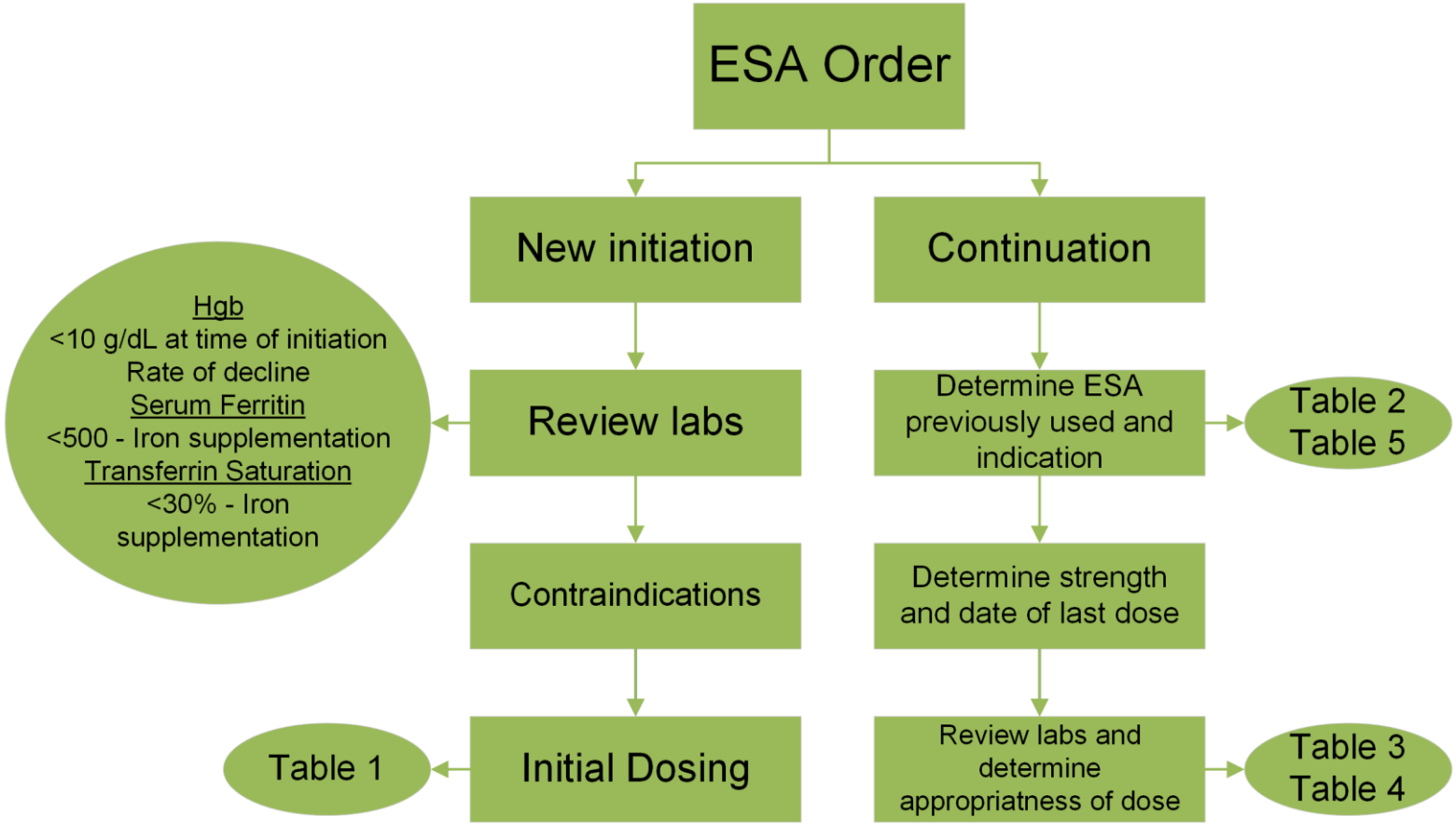

Table 1: Initial Dosing
Table 2: FDA Approved Indications
Table 3: Dose Adjustment Guide
Table 4: Time Required before Dose Adjustment
Table 5: Mircera Dose Conversions
Table 6: Changing ESA based on Dosing
Table 7: Iron Supplementation

*The standard work aligns with current prescribing and dosing guidelines from the FDA, KDIGO, and NCCN

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Population Results

	Control			Case			All Encounters		
Age Group	**Female**	**Male**	**Total**	**Female**	**Male**	**Total**	**Female**	**Male**	**Total**
<65	8	10	18	10	10	20	18	20	38
65-80	19	22	41	8	18	26	27	40	67
>80	7	9	16	5	3	8	12	12	24
Grand Total	34	41	75	23	21	54	57	72	**129**
%	45.3%	54.7%		42.6%	57.4%		44.2%	55.8%	

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Preliminary Results

Number of Patients	129
Number of Hospitalizations	151
Total Doses Administered	
Control	110
Case	81
Total	191

Conclusion

- Conclusion
  - Number of ESA doses administered after the standard work implementation decreased
  - ESA Standard Work Policy provides pharmacists with a guide to appropriate dosing and prescribing and allows for improved identification of inappropriate doses
- Limitations
  - Small sample size
  - Retrospective chart review
  - Lack of randomization
  - Single center design

Assessment Question

What are some of the risks associated with ESA administration that make appropriate dosing and prescribing so important?

A. Increased risk of thromboembolic events
B. Increased risk of mortality
C. Increased risk of cardiovascular events
D. Increased risk of tumor progression
E. All of the above

Assessment Question

The implementation of an ESA standard work policy provides an opportunity to improve the rates of appropriate ESA dosing and prescribing in the hospital setting?

A. True

B. False

ACKNOWLEDGMENTS

- Research Mentors:
  - Elizabeth Monson, PharmD, BCPS
  - Brianna Kempema Nelson, PharmD, BCPS
  - Irina Haller, PhD, MS
  - Colleen Renier, BS

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Examining The Impact of a Pharmacist-Managed Diabetes Care Program in an Internal Medicine Clinic: A Retrospective Matched Cohort Study

Fatme Younes, PharmD
PGY1 Pharmacy Resident
Sanford Medical Center Fargo

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Disclosures

- The speaker has no actual or potential conflict of interest in relation to this presentation

Learning objective

Learning Objective

- Evaluate the impact of a pharmacist-managed diabetes care program in place at Sanford Health Internal medicine clinics in Fargo, ND and Moorhead, MN

Background

Background

- Pharmacist-Managed Diabetes Care Program (PMDCP)
  - First introduced to Sanford Health in Fargo in 2013
  - Currently in both family and internal medicine clinics in Fargo, ND and Moorhead, MN
- Since the program's inception, internal data have been analyzed to determine patients' change in A1C from the time the patient is referred to the time the consult is ended
- However, data had not yet been compared to outcomes in patients not referred to the program

Literature Review

- CDC's 2022 estimates
  - Total # of people with diabetes: 38.4 million people
  - US adults: 14.7%
  - ≥ 65 years old: 29.2%
- American Diabetes Association recommendation:
  - A1C goal of < 7% in most non-pregnant adults
  - ↓ rates & progression of micro-vascular and macro-vascular complications
- Chronic condition management and prevention services
  - CDC has recognized pharmacists medication expertise and the potential for expanded access to care through CPAs

Ann Pharmacother. 2017
Diabetes Care. 2024
National Diabetes Statistics Report. 2022

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Study Objective

To compare outcomes of patients with diabetes enrolled in a Pharmacist-Managed Diabetes Care Program (PMDCP) with similar patients receiving usual medical care (UMC) independent of clinical pharmacy services

Methods

Study design

Single center retrospective matched cohort study

- Sanford Internal Medicine Clinics
- 2018-2020

Enterprise Data Analytics (EDA) Report

- Manual Chart Review

Sanford IRB Approved

Study design

Inclusion Criteria

- Age ≥18 years
- Type 1 or type 2 diabetes mellitus
- Initial HbA1C ≥ 8%
- ≥1 intervention made by the pharmacist OR ≥ 1 office visit with an internal medicine provider between July 1, 2018 and June 30, 2020
- Received primary care at Sanford South Pointe, Broadway, or Moorhead internal medicine clinics during the specified time frame

Exclusion Criteria

- Pregnancy
- Endocrinology consult
- Pharmacist referral placed for hypoglycemia management
- No follow-up A1C drawn within 12 months of the index date
- Initial A1C drawn > 6 months prior to the pharmacist referral date

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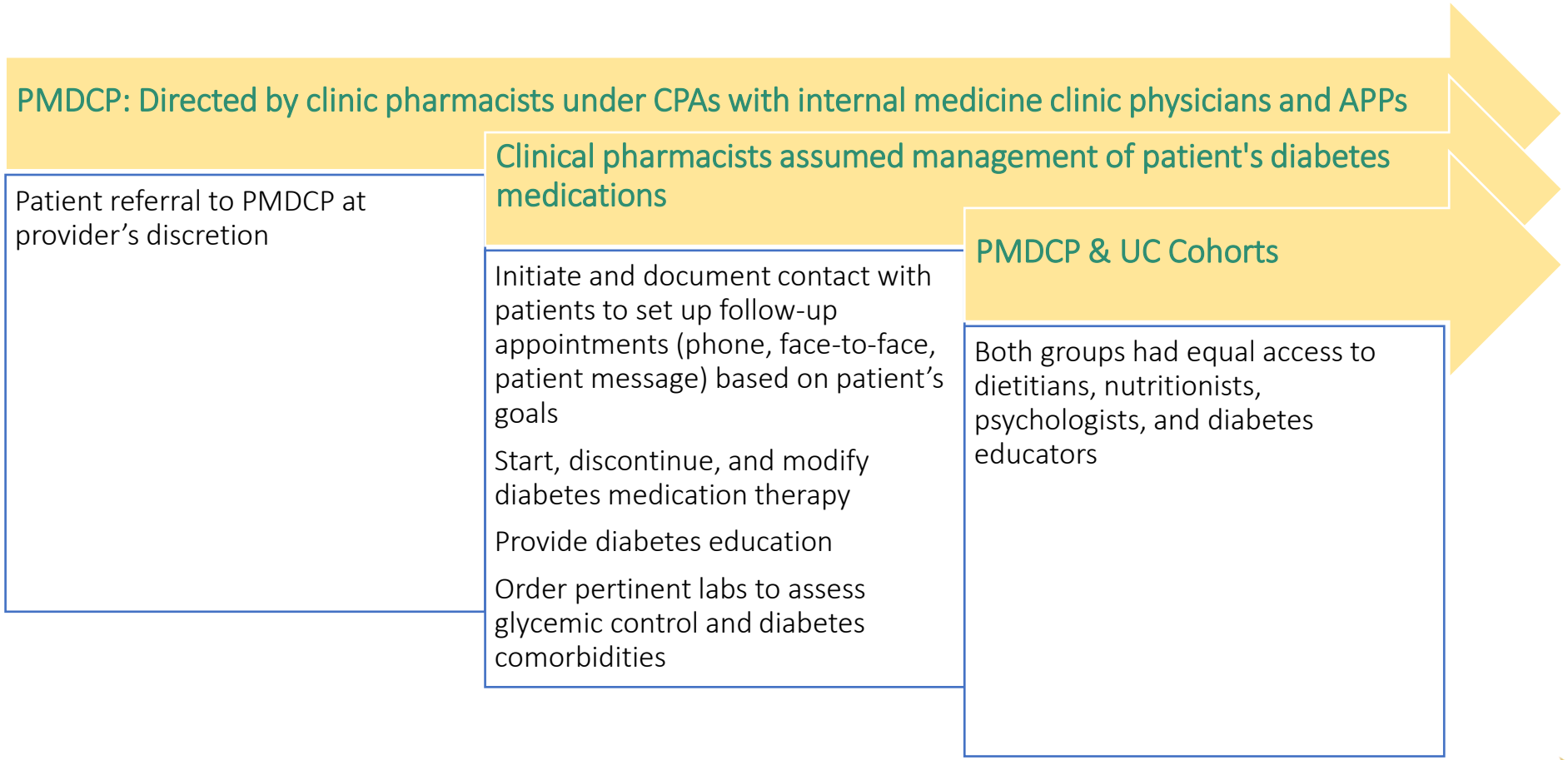
Study design



Outcomes

Primary Outcome

- Mean reduction in A1C at 12 months

Secondary Outcome

- Percentage of patients reaching A1C < 7% at 12 months

Statistics

- Chi-square tests were used to compare categorical data
- Wilcoxon rank sum test was used to compare continuous data

Results

Population Characteristics

	Pharmacist-Managed Diabetes Care (N= 158)	Usual Medical Care (N= 158)
Mean Age (years)	61.7	61.8
Gender		
• Male	68	72
• Female	90	86
Diabetes Type		
• Type 1	3	6
• Type 2	155	152
Mean Initial A1c (%)	9.81	9.85
Comorbidities		
• Hypertension	132	130
• Stroke	9	7
• Chronic Kidney Disease	35	67
• History of MI	13	14
• Ischemic Heart Disease	83	59
• Coronary Artery Disease	38	35

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Results

	Pharmacist-Managed Diabetes Care (N= 158)	Usual Medical Care (N= 158)	Between-group difference	P value
Primary Outcome				
• Mean Change in A1c at 12 months	-1.70%	-1.31%	0.39%	0.0073
Secondary Outcome				
• Percentage of patients achieving A1c < 7% at 12 months	24.6%	22.8%	1.8%	0.6916

Discussion

Limitations

- **Retrospective study design**
  - Accuracy of the data obtained reliant on the accuracy of the documentation in the EMR
  - Lack of randomization allows for the possibility of confounding
  - While the PMDC and UMC groups were similar in most characteristics and comorbidities evaluated, it is impossible to eliminate all confounding variables
  - Timeframe of the diabetes diagnosis (new versus remote diagnosis) as well as the diabetes medication therapies used (class and number of medications) could have influenced the study outcomes

- **Study not powered to detect a difference in the secondary outcome**
  - Could explain no statistical significance
  - Another explanation may have to do with the fact that a A1c goal of < 7% is not only difficult to reach but it is also not appropriate for everyone

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Conclusion

Conclusion

- Addition of a pharmacist-managed care for patient with diabetes is associated with significant improvements in A1C compared with usual care alone
- The percentage of patients in the pharmacist-managed care group who reached A1C of < 7% was similar to the patients undergoing usual care
- Our results support the implementation of pharmacists into diabetes management teams

Acknowledgments

Research Mentors

- Nick Meyer, PharmD
- Douglas Gugel-Bryant, PharmD, BCPS
- Carlina Grindeland, PharmD, BCPS, BCPPS

Questions?

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A Retrospective Comparison of Opioid Medication Choice for the Treatment of Neonatal Iatrogenic Withdrawal

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PGY1 Pharmacy Resident
Sanford Medical Center Fargo

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Disclosures

The speaker has no actual or potential conflict of interest in relation to this presentation.

United States' largest not-for-profit rural healthcare system

Sanford Health includes:
46 medical centers
210 clinic locations
208 senior living communities
158 skilled nursing and rehab facilities

Centers of Excellence:
Cancer
Children's
Heart
Orthopedics/Sports Medicine
Women's Health

Each year provides:
5.5 million outpatient and clinic visits
212,077 emergency department visits
88,368 admissions
140,510 surgeries and procedures
9,602 births

Learning objective

Understand the use and utility of morphine and methadone for iatrogenic withdrawal weaning in the neonatal population

Pre-assessment question

- True or false: Methadone and morphine can be used to treat neonatal iatrogenic withdrawal

Background

Background

- Over 3.6 million births in 2021, with an estimated 9-13% rate of needed admission to the neonatal intensive care unit (NICU)
- Neonates have the ability to feel pain with that pain generally dysregulated due to lack of neural pathway maturation
- Since poorly controlled pain leads to negative impacts on brain development, pain medication (specifically opioids) are used commonly in the NICU
- Opioid use may negatively impact infant brain development, as well as create withdrawal risk when discontinued

Literature Review

Cramton and Gruchala (2013)	Neonatal iatrogenic withdrawal is complex and lacks consistent definitions and standard treatments
Robertson et al (2000)	Methadone can be used for weaning pediatric patients from opioids after prolonged use
Steineck et al (2014)	Pharmacist protocolized methadone tapers result in shorter and less opioid exposure

Study Objective

- This study looks to investigate optimal opioid withdrawal treatment in neonates admitted to the neonatal intensive care unit by comparing opioid total exposure between neonates after being treated with more than 5 consecutive days of continuous opioid infusions or scheduled opioid administrations. They were then weaned using methadone or morphine to determine if one medication resulted in less total morphine milliequivalents per kilogram exposure, side effects, and more favorable outcomes.

Methods

Study Design

- Single-centered, retrospective cohort trial of patients admitted to the NICU with the use of continuous or scheduled opioids for 5 or more days consecutively and required opioid wean

Study Design

Inclusion Criteria

- Gestational age < 37 weeks
- Scheduled or continuous opioid used for at least 5 consecutive days
- Admitted to the Sanford Fargo NICU

Exclusion Criteria

- Trisomy 21
- Trisomy 18
- Patients who expired during sedation or taper
- Patients who transferred hospital systems
- Diagnosis of neonatal abstinence syndrome or in utero drug exposure

Data Collection

Baseline Data

- Gestational Age
- Race
- Sex
- Singleton or Multiple
- Comorbidities

Clinical Data

- WAT-1 scores
- NAPSS scores
- Daily opioid usage
- Adjunct agent administration

Primary Outcomes

Total dose exposure of opioid medications (MME/kg)

Secondary Outcomes

Hypoxic-Ischemic Encephalopathy (HIE)

Intraventricular Hemorrhage (IVH)

Periventricular Leukomalacia (PVL)

Necrotizing Enterocolitis (NEC)

Results

Population (N=29)

Variable	Morphine	Methadone	P-value
Average gestation (weeks-days)	26-3	25-2.5	0.559
Sex (male)	10 (34.48%)	12 (41.38%)	0.1388
Singleton	7 (24.14%)	14 (48.28%)	0.7146
Average weight	1.928	1.185	0.0836
Race (white)	6 (20.69%)	8 (27.59%)	0.3964
Continuous Infusion Agent (fentanyl)	10 (34.48%)	14 (48.28%)	0.1211

Primary Outcome

Variable	Morphine	Methadone	P-value
Infusion Agent Total (MME/kg/day)	56.46	149.39	0.0183*
Infusion Agent Average (MME/kg/day)	6.76	9.32	0.1568
Taper Agent Total (MME/kg/day)	3.53	80.07	<0.0001*
Taper Agent Average (MME/kg/day)	0.31	3.96	<0.0001*
On Concurrent $Alpha_2$ Agonist	9 (31.03%)	13 (44.83%)	0.5579
On Concurrent Benzodiazepine	0	3 (10.34%)	0.1527

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Primary Outcome

Variable	Morphine	Methadone	P-value
Average Duration of Taper	10	20.5	0.0141*
Average Duration of Infusion	10	15.5	0.0402
Difference between Taper and Infusion Days	-1	1	0.3003

Secondary Outcomes

Variable	Morphine	Methadone	P-value
Incidence of IVH	4 (13.79%)	5 (17.24%)	0.6277
Incidence f NEC	2 (6.9%)	1 (3.45%)	0.2787
Incidence of PVL	2 (6.9%)	1 (3.45%)	0.2787
Incidence of HIE	0	2 (6.9%)	0.2519

Discussion

Findings Summary

No difference between baseline characteristics

Significant difference between morphine and methadone MME/kg/day exposure

Differences in duration of tapering agent when compared to length of continuous infusion

Limitations

Limitations

- Variable opioid conversions
- Retrospective, small sample size
- Single center
- Charting errors

Conclusion

Conclusions

Regarding the use of morphine or methadone for iatrogenic weaning from continuous opioid infusions, the use of morphine when compared to methadone significantly decreased the amount of opioid exposure quantified in morphine miliequivalents/kilogram/day.

Acknowledgments

- Research Mentors: Carlina Grindeland, Julia Muzzy

Post-Assessment Question

- True or false: Methadone and morphine can be used to treat neonatal iatrogenic withdrawal?

Questions

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Glucagon-Like Peptide 1 Agonist Impact on Inflammatory Bowel Disease

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Disclosures

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Women's Health

Each year provides:
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212,077 emergency department visits
88,368 admissions
140,510 surgeries and procedures
9,602 births

Learning objective

- Describe the mechanisms and pathophysiology of inflammatory bowel diseases.
- Identify current and new therapy options for inflammatory bowel disease.

Pre-assessment question

Which medication is NOT currently an approved treatment for inflammatory bowel diseases?

A. Methotrexate
B. Adalimumab
C. Semaglutide
D. Tofacitinib

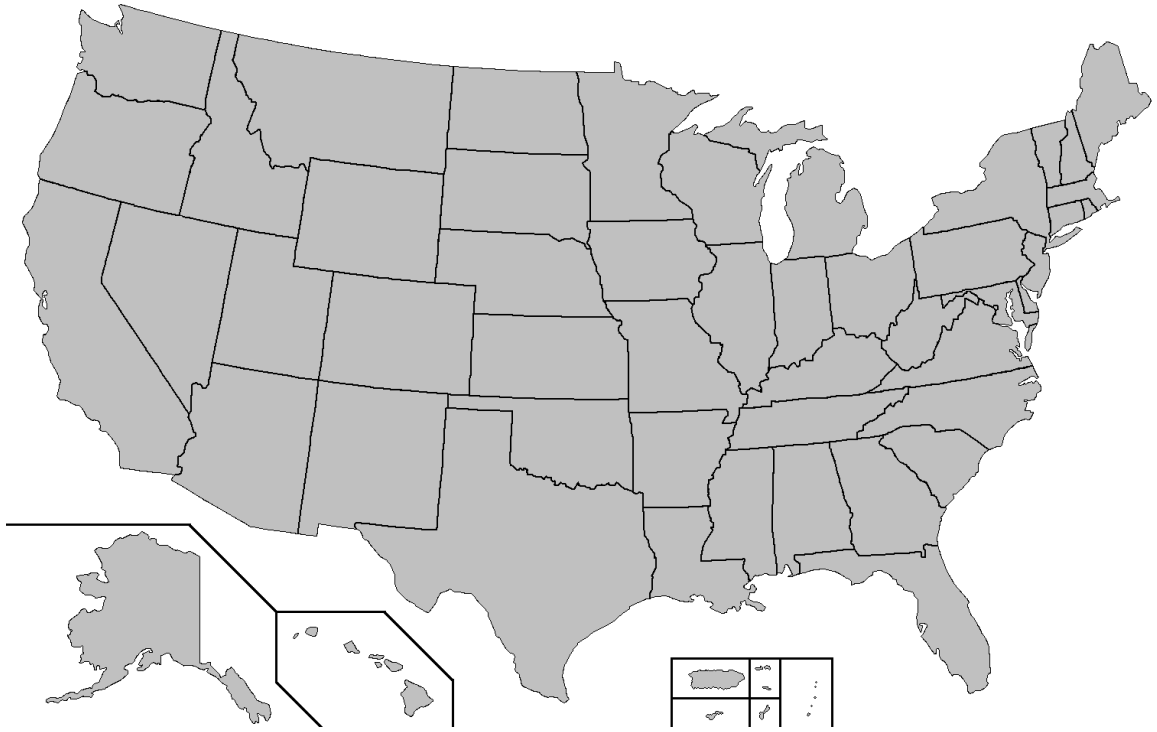
Background

Background

3.1 Million Americans

$25.4 Billion in 2016

Pharmacist Role



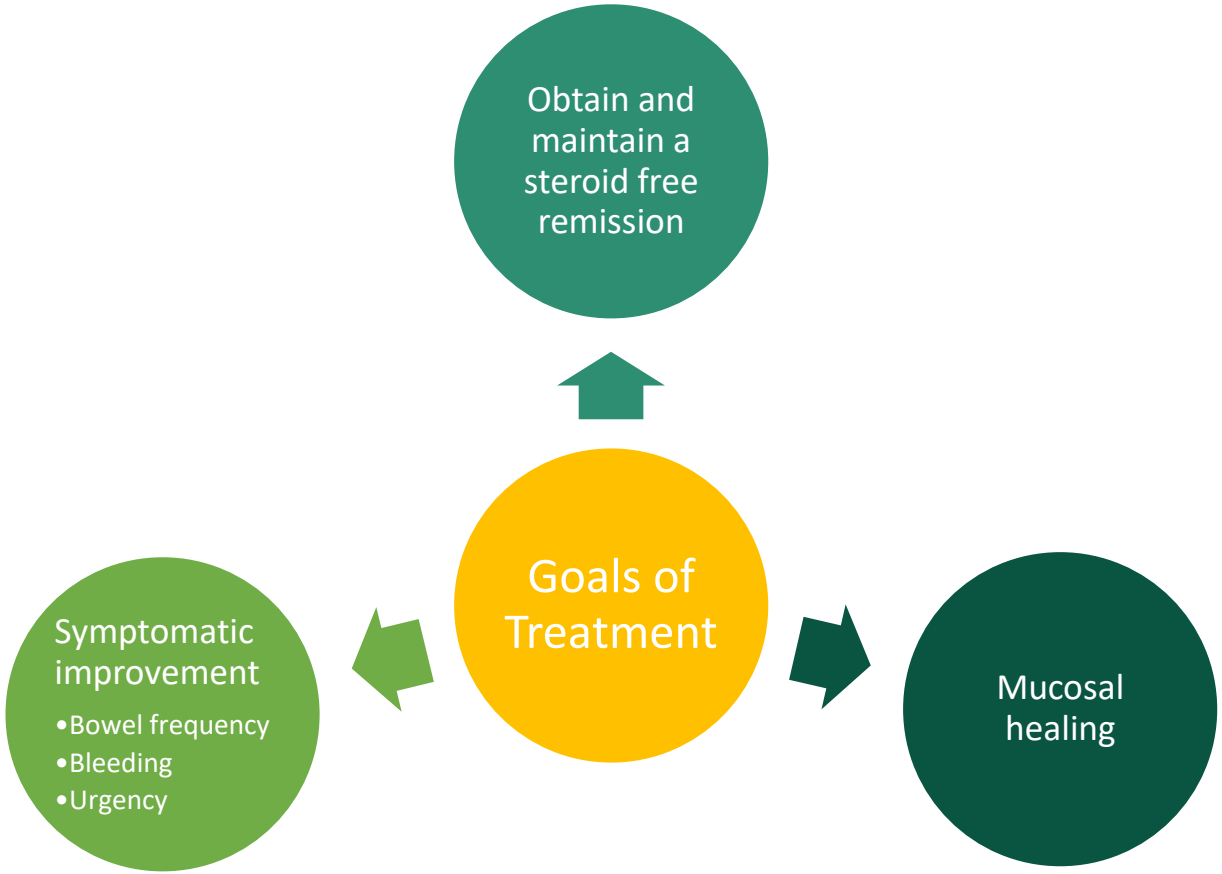
Kappelman et al. *Digestive Diseases and Sciences*. 2013.
Singh, et al. *Inflammatory Bowel Disorders*. 2022.
Prasad, et al. *Pharmacy (Basel)*. 2020.

Inflammatory Bowel Disease

Crohn’s Disease

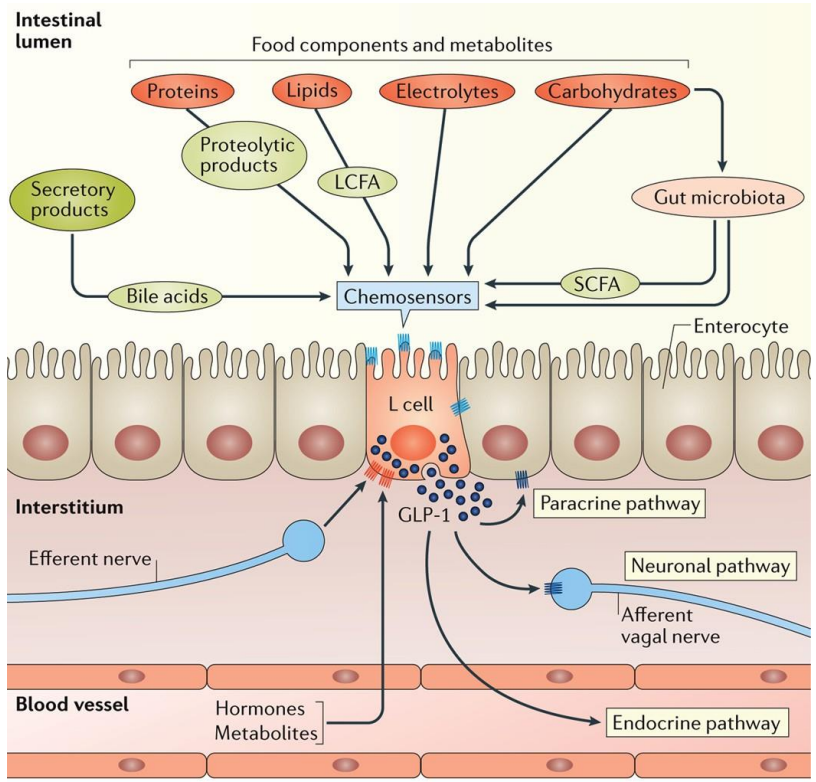
Ulcerative Colitis

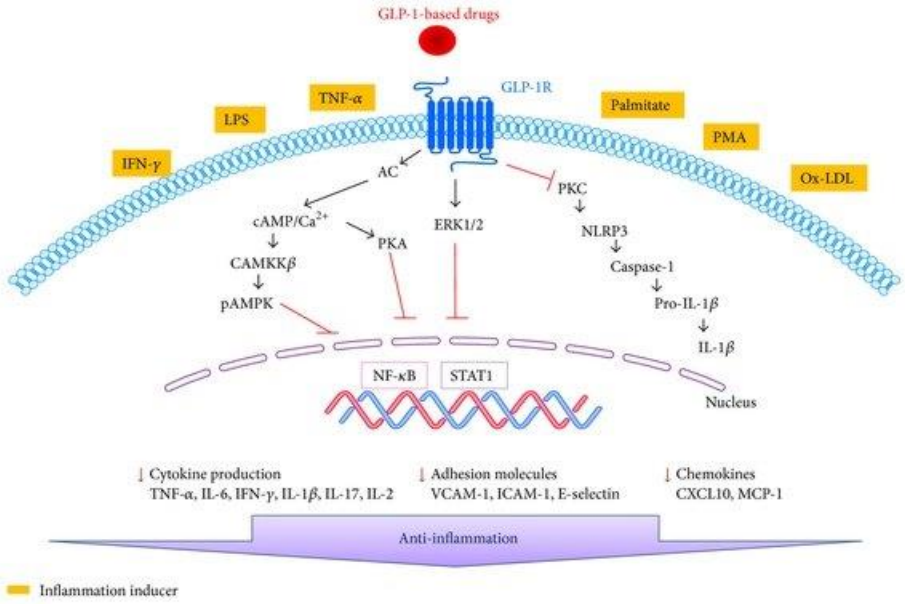
Treatment


Obtain and maintain a steroid free remission
Goals of Treatment
Symptomatic improvement
•Bowel frequency
•Bleeding
•Urgency
Mucosal healing

Medication	Mechanism
5 Amiosalicyclic-acid	
Sulfasalazine	Cyclooxygenase pathway modulation
Mesalamine	
Corticosteroids	
Budesonide	Depress activity of endogenous pro-inflammatory mediators
Prednisone	
Methylprednisolone	
Immunomodulators	
Azathioprine/6-mercaptopurine	Incorporated into DNA replication cycle, blocking purine synthesis
Methotrexate	Inhibits dihydrofolic acid reductase, interfering with DNA synthesis, repair, and replication
TNFα Inhibitors	
Inflixamab	Monoclonal antibody that binds to tumor necrosis factor alpha (TNFα), reducing induction of pro-inflammatory cytokines, leukocyte migration, activation of neutrophils and eosinophils
Adalimumab	
Certolizumab-Pegol	
Golimumab	
α4β7 Integrin Inhibitor	
Vedolizumab	Monoclonal antibody that binds to α4β7 integrin blocking interaction with mucosal addressin cell adhesion molecule-1, which inhibits migration of lymphocytes into inflamed tissue
IL-12, IL-23 Inhibitor	
Ustekinumab	Monoclonal antibody that binds to IL-12 and IL-23, interfering with NK cell activation, T cell differentiation and activation.
Janus Kinase Enzyme Inhibitor	
Tofacitinib	Inhibits Janus kinase (JAK) enzymes, interfering with cytokine or growth factor expression in immune cells
Upadacitinib	

Glucagon like peptide – 1 (GLP-1)





Lee, et al. *Mediators of Inflammation*. 2016.
Muskiet, et al. *Nature Reviews Nephrology*. 2017

GLP-1 Receptor agonists

Dulaglutide	• Once weekly
Liraglutide	• Once daily
Semaglutide	• Subcutaneously = Once weekly • Oral = Once daily
Exenatide	• Twice daily OR once weekly (two subcutaneous formulations)
Tirzepatide	• Once weekly • Dual MOA: Glucose dependent insulinotropic polypeptide (GIP) and GLP-1

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Literature Review

Research paper

GLP-1 based therapies and disease course of inflammatory bowel disease

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[c] *Copenhagen Phase IV unit (Phase4CPH), Department of Clinical Pharmacology and Center of Clinical Research and Prevention, Bispebjerg and Frederiksberg Hospital, Copenhagen, Denmark*
[d] *Center for Molecular Prediction of Inflammatory Bowel Disease, Department of Clinical Medicine, Aalborg University, Copenhagen, Denmark*

Villumsen, et al. *EClinicalMedicine*. 2021.

Literature Review

Table 2
IRRs of composite and specific outcomes comparing treatment with GLP-1 receptor agonists/DPP-4 inhibitors with other antidiabetic therapies.

	New users of GLP-1-receptor agonists and/or DPP-4 inhibitors			Non-users of GLP-1-receptor agonists and/or DPP-4 inhibitors			Crude estimate	Adjusted estimate
Composite outcome	Events	PY	IR per 1000 PY	Events	PY	IR per 1000 PY	IRR (95% CI)	IRR (95% CI)
Total	199	1861	106·9	2333	9652	241·7	0·44 (0·38–0·51)	0·52 (0·42–0·65)
Sex								
Female	50	344	145·1	1079	4325	249·5	0·44 (0·35–0·54)	0·49 (0·35–0·69)
Male	149	1517	98·2	1235	5202	237·4	0·45 (0·37–0·55)	0·55 (0·41–0·73)
IBD subtype								
CD	90	836	107·6	640	2144	298·5	0·49 (0·36–0·65)	0·62 (0·41–0·92)
UC	109	1025	106·3	1674	7382	226·8	0·43 (0·37–0·51)	0·50 (0·39–0·65)
Separate outcomes								
Hospitalisation	178	2889	61·6	1445	14,024	103·0	0·60 (0·51–0·70)	0·73 (0·58–0·91)
Surgery	97	3675	26·4	593	17,456	34·0	0·78 (0·63–0·96)	0·79 (0·57–1·09)
Steroid initiation	133	2813	47·3	1238	13,104	94·5	0·50 (0·42–0·60)	0·54 (0·41–0·70)
TNF-α-inhibitor initiation	29	4183	6·9	213	18,737	11·4	0·61 (0·41–0·90)	0·56 (0·32–1·00)

CD Crohn's disease, CI confidence interval, IR Incidence rate, IRR Incidence Rate Ratio, PY Person Years, TNF-α tumour necrosis factor alpha, UC Ulcerative Colitis.

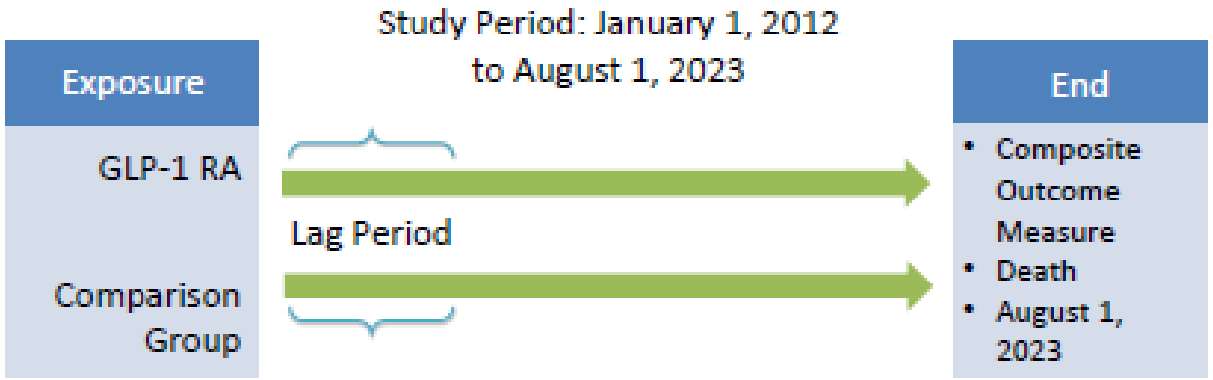
Villumsen, et al. *EClinicalMedicine*. 2021.

Study Objective

What is the impact of GLP-1 receptor agonist medications on inflammatory bowel disease?

Methods

Study Design



- Population level reports through the electronic healthcare record
- Extensive chart review of the electronic healthcare record
- Lag period to eliminate potential pre-study impacts

Outcomes

Primary Outcome

- Incidence rate of need for oral corticosteroid treatment, need for TNF a inhibitor treatment, IBD related hospitalization, or IBD related major surgery post initiation of GLP 1 agonist.

Secondary Outcomes

- Individual components of composite outcomes
- Percentage of patients that reached normalization of fecal calprotectin (≤ 50 mcg/g) or CRP(≤ 0.8 mg/dL) post initiation of GLP-1 agonist

Results

Population

Inclusion

- Sanford Health enterprise patients
- Diagnosis of Crohn’s disease OR ulcerative colitis, AND type 2 diabetes
- GLP-1 receptor agonist use during collection period

Exclusion

- Diagnosis of type 1 diabetes
- Pregnancy
- Hyper-sensitivity to GLP-1 medications

Population

	Treatment Group		Control Group	
	N	%	N	%
General characteristics	101		73	
Sex				
Female	53	52.5	32	43.8
Male	48	47.5	41	56.2
Age at study entry	55.29 years		55.37 years	
IBD related characteristics				
Crohn's Disease	48	47.5	29	39.7
Ulcerative Colitis	53	52.5	44	60.3

Primary Outcome

	Treatment Group			Control Group				
	Events	PY	IR per 1000 PY	Events	PY	IR per 1000 PY	IRR (95% CI)	P value
Composite Outcome								
Total	33	297.14	111.06	21	321.81	65.26	1.70 (0.98-2.94)	0.054
Separate Outcomes								
Hospitalization	8	302.00	26.49	5	329.66	15.17	1.75 (0.57-5.34)	0.058
Surgery	1	297.13	3.37	5	324.75	15.40	0.22 (0.03-1.87)	0.0004
Steroid initiation	24	302.91	79.23	14	330.90	42.31	1.87 (0.97-3.62)	0.13
TNF alpha inhibitor initiation/escalation	12	303.04	39.60	9	324.18	27.76	4.19 (1.77-9.40)	0.32

Secondary Outcomes

	Treatment Group	
	Initial	Normalized (%)
C-Reactive Protein	87	53 (60.9)
Fecal Calprotectin	35	12 (34.3)

Discussion

Conclusions

- The treatment group exhibited a higher incidence rate per 1000 person years of the composite outcome.
- Steroid initiation was the individual outcome that had the most influence on the composite.
- CRP and FC are potential biomarkers for tracking IBD.

Limitations

- Electronic healthcare record
- Multiple hospital systems
- Matched cohort
- Small sample size
- Emerging treatment options for IBD

Acknowledgments

- Research Mentors:

  Douglas Gugal-Bryant, PharmD, BCPS
  Carlina Grindeland, PharmD, BCPPS

Post-Assessment Question

Which medication is NOT currently an approved treatment for inflammatory bowel diseases?

A. Methotrexate
B. Adalimumab
C. Semaglutide
D. Tofacitinib

Post-Assessment Question

Which medication is NOT currently an approved treatment for inflammatory bowel diseases?

A. Methotrexate

B. Adalimumab

C. Semaglutide

D. Tofacitinib

Questions

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Pharmacy Residency Research Showcase

Break Time

Session 2 begins at 3:00 pm in this same room

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Session 2

- Evaluation of a Pharmacist-led Emergency Department Culture Review Program in an Upper Midwest Mid-Sized Community Hospital; Tony A. Maanum, PharmD
- Impact of Ongoing Provider Feedback and Education on Antibiotic Prescribing for Upper Respiratory Tract Infections in the Urgent Care Setting; Abilene Leitch, PharmD
- Early Use Milrinone for Vasospasm Prevention in Aneurysmal Subarachnoid Hemorrhage; Cameron Sofia, PharmD
- Phenylephrine vs. Norepinephrine in ICU Shock Patients in Atrial Fibrillation with Rapid Ventricular Rate; Trenton LaCanne, PharmD

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Evaluation of a Pharmacist-led Emergency Department Culture Review Program in an Upper Midwest Mid-Sized Community Hospital

Tony Maanum, PharmD

PGY1 Pharmacy Resident

Essentia Health Fargo Hospital

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Disclosures

- Authors of this presentation have nothing to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation

Objectives

- Determine if time to appropriate therapy is different between a pharmacist-led ED culture review compared to a physician-led ED culture review

- Describe the impact of a pharmacist-led ED culture review in a mid-sized community hospital

Background

- Culture review in the Emergency Department has been a hallmark of ED care for many years
- Professions that have been providing this care has changed over recent years
- Providers, nurses, infection prevention, and pharmacists have been utilized to provide ED culture review

Previous Data Results

- Higher percentage and number of interventions
- Decreased rehospitalization rates
- Faster time to appropriate therapy
- Improved management of multi-drug resistant pathogens

Implementation

- Originally managed by ED providers at Essentia Health
- Pharmacists would frequently assist with management and antibiotic recommendations
- Pharmacists took over responsibility of this process in January 2023 with support from the ED provider team

Methods

- Design: Historical single-center case control

- Study period:
  - Case group: May – November 2023
  - Control group: May – November 2022

- Retrospective comparison between provider managed patients to pharmacist managed patients

Patient Population

Inclusion Criteria	Exclusion Criteria
• Emergency Department Patients • Age 18+ years • Wound, respiratory, urinary cultures, or sexually transmitted infection test	• Patients who were admitted to the hospital • Patients who returned to the hospital within 72 hours

Outcomes

- Primary Outcome
  - Time until appropriate antibiotic therapy

- Secondary Outcomes
  - Amount of patients receiving this service
  - Total time spent providing this service
  - Antibiotic prescribing patterns and changes made by pharmacists

Data Collection

- Patient data was obtained for the case and control group from the electronic health record and de-identified for analysis
- Analysis of intervention was antibiotic change in discharge patients determined by receipt of a new antibiotic prescription after culture results
- Analysis of time saved was determined by ODB marker time classification and total number of interventions made

Statistical Analysis

- Primary outcome analysis
  - If normally distributed: Generalized estimated equations (GEE) linear models
  - Not normally distributed: GEE analysis of RANKS model

- Secondary outcome analysis
  - GEE binary logistic regression
  - Descriptive analysis

Limitations

- Retrospective
- Single center
- Lack of randomization
- Changes in processes and procedures from the 1-year difference between groups could confound the outcomes
- Some patients could not be reached by pharmacists during the call back process

Population Information

- 812 patients which accounted for 905 total ED encounters matching the specified criteria
- The control group accounted for 436 encounters and 469 encounters were in the case group
- Of the 812 total patients, 654 were female and 158 were male
- Age was also broken down with 177 patients with age <30, 229 patients with age 31-49, 221 patients with age 50-74, and 185 patients with age >75

ACKNOWLEDGMENTS

- Research Mentors:
  - Jennifer Catlin, PharmD, BCPS, BCCCP
  - Sydney Armbrust, PharmD, BCPS
  - Colleen M. Renier, BS
  - Irina V. Haller, PhD, MS

Question #1

What are some of the potential benefits that have been seen in previous studies?

1. Increased number of interventions
2. Improved therapy of resistant bacteria
3. Decreased rehospitalization rates
4. Faster time to appropriate therapy
5. All of the above

Question #2

The implementation of a pharmacist-led ED culture review provides an opportunity to improve time to appropriate therapy for patients discharged from the ED with an infection?

1. True
2. False

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Thank you!

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Impact of Ongoing Provider Feedback and Education on Antibiotic Prescribing for Upper Respiratory Tract Infections in the Urgent Care Setting

Abilene Leitch, PharmD
PGY1 Pharmacy Resident
Sanford Medical Center Fargo

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DISCLOSURES

The speaker has no actual or potential conflict of interest in relation to this presentation.

United States' largest not-for-profit rural healthcare system

Sanford Health includes:
46 medical centers
210 clinic locations
208 senior living communities
158 skilled nursing and rehab facilities

Centers of Excellence:
Cancer
Children's
Heart
Orthopedics/Sports Medicine
Women's Health

Each year provides:
5.5 million outpatient and clinic visits
212,077 emergency department visits
88,368 admissions
140,510 surgeries and procedures
9,602 births

LEARNING OBJECTIVE

At the completion of this activity, the participant will be able to:

- Evaluate the appropriateness of antibiotics for upper respiratory tract infections in the urgent care setting

PRE-ASSESSMENT QUESTION

True or False: Antibiotics are always indicated for acute upper respiratory tract infections.

BACKGROUND

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BACKGROUND

- In 2020, Joint Commission enacted standards for antimicrobial stewardship in the ambulatory care setting.
- A recent survey of the current state of ambulatory ASPs revealed only 7% were fully functional.
- Respiratory tract infections (RTIs) present an ideal initial target of antimicrobial stewardship efforts in the clinic, as the condition is highly prevalent in this setting, and antibiotics are often prescribed despite likely viral etiologies.
  - A 2022 study of nearly 50,000 upper RTI encounters showed 42.4% resulted in an unnecessary antibiotic prescription.

Chandra Deb L, et al. *Open Forum Infect Dis.* 2022;9(7):ofac302.
Eudy JL, et al. *Open Forum Infect Dis.* 2020;7(11):ofaa513.
The Joint Commission. 2023.

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LITERATURE REVIEW

Schwartz et al (2021)

- Mailed high-prescribing PCPs a letter with recommendations for antibiotic initiation or prescribing duration
- Letter with duration recommendations led to fewer antibiotics and fewer prolonged-duration antibiotics compared to no letter
- No difference for letter about initiation of antibiotics

Dutcher et al (2022)

- Initial education session followed by monthly electronic feedback
- Reduced overall antibiotic prescribing

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Dutcher L, et al. *Clin Infect Dis.* 2022;74(6):947-956.
Schwartz KL, et al. *JAMA Int Med.* 2021;181(9):1165-1173.

STUDY OBJECTIVE

To assess the impact of feedback via provider report cards and education on antibiotic prescribing for upper respiratory tract infections in the urgent care setting.

METHODS

STUDY DESIGN

Inclusion

- Sanford Health Fargo urgent care clinics
- Encounters with ICD-10-CM codes for acute upper respiratory tract infections, bronchitis, or pharyngitis without a positive Group A *Streptococcus* test (“never” indications)

Exclusion

- Age < 18 years old
- Non-oral antibiotics
- Problem list and 30-day indications to exclude patients who may have required antibiotics for another reason

STUDY DESIGN (CONT.)

Antibiotic prescribing data collected via electronic algorithm

Appropriate care rate calculated for each "never" indication

Report cards and educational resources emailed to each provider plus periodic educational meetings

- **Appropriate care rate:** percentage of encounters with "never" indications and no antibiotic prescribed
- **Statistical analysis:** multi-level mixed effects regression model based upon a generalized linear model with separate models fit for each secondary outcome

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STUDY DESIGN (CONT.)

Provider Specialty: PA - Family Medicine

Provider Type: Physician Assistant

Measures	Provider rate for Appropriate Care (Ideal = 100%)	Average Rate for Peers (Department)	Average Rate for Peers (Provider Type)	Quintile Rank (Department)	Quintile Rank (Provider Type)	Total Encounters
Acute Bronchitis	NS	55.58%	43.48%	NS	NS	6
Pharyngitis	100.00%	89.78%	83.22%	1	1	17
Acute URI	100.00%	86.18%	71.51%	1	1	30
Composite	92.68%	81.72%	71.15%	2	1	53

Provider Specialty: NP - Family Medicine

Provider Type: Certified Nurse Practitioner

Measures	Provider rate for Appropriate Care (Ideal = 100%)	Average Rate for Peers (Department)	Average Rate for Peers (Provider Type)	Quintile Rank (Department)	Quintile Rank (Provider Type)	Total Encounters
Acute Bronchitis	0.00%	55.58%	30.40%	4	4	68
Pharyngitis	56.82%	89.78%	85.14%	5	4	44
Acute URI	75.00%	86.18%	80.30%	5	4	12
Composite	28.57%	81.72%	68.57%	5	4	124

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OUTCOMES

Primary Outcome

- Change in ACR between pre- and post-intervention groups for composite scores

Secondary Outcomes

- Change in ACR for each “never” indication
- Change in composite ACR by provider type

RESULTS

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POPULATION

- 2 Sanford Fargo urgent care clinics

- 17 providers included in the analysis
  - Four physician associates
  - Four certified nurse practitioners
  - Nine physicians

- 7259 encounters in the pre-intervention period
- 6077 encounters in the post-intervention period

PRIMARY OUTCOME

Composite appropriate care rate for upper respiratory tract infection antibiotic prescribing in the pre- and post-intervention periods.

Appropriate Care Rate	Pre-Intervention		Post-Intervention		t-test	p-value
	N	Mean (SD)	N	Mean (SD)		
Composite	179	0.76 (0.19)	172	0.79 (0.21)	-1.79	0.037

Mixed effects model for composite appropriate care rate for antibiotic prescribing.

Appropriate Care Rate	β	Standard Error	Z	p-value	95% CI	
Intervention, pre=0, post=1	0.083	0.042	2	0.045	0.002	0.164

PRIMARY OUTCOME

Composite appropriate care rate for upper respiratory tract infection antibiotic prescribing in the pre- and post-intervention periods.

Appropriate Care Rate	Pre-Intervention		Post-Intervention		t-test	p-value
	N	Mean (SD)	N	Mean (SD)		
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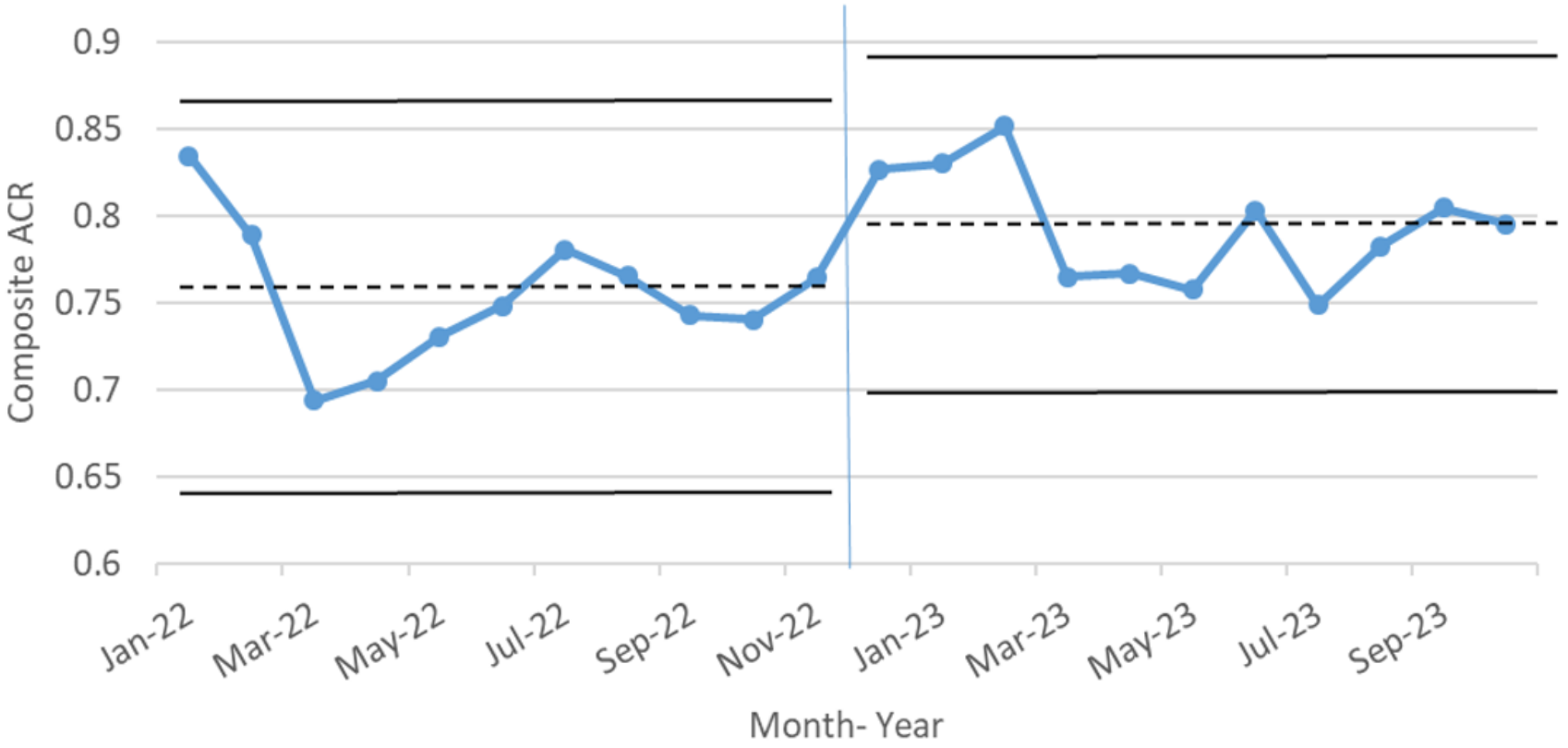
Intervention, pre=0, post=1	0.083	0.042	2	0.045	0.002	0.164

MIXED EFFECTS MODEL – COMPOSITE ACR



Abbreviations: ACR, appropriate care rate; Jan, January; Mar, March; Jul, July; Sep, September; Nov, November.

SECONDARY OUTCOMES

Appropriate care rates for upper respiratory tract infection antibiotic prescribing in the pre- and post-intervention periods by diagnosis.

Appropriate Care Rate	Pre-Intervention		Post-Intervention		t-test	p-value
	N	Mean (SD)	N	Mean (SD)		
AURI	179	0.82 (0.19)	172	0.85 (0.20)	-1.37	0.085
Bronchitis	151	0.39 (0.40)	139	0.49 (0.41)	-2.05	0.021
Pharyngitis	179	0.84 (0.20)	172	0.86 (0.20)	-0.71	0.239

Abbreviation: AURI, acute upper respiratory tract infection.

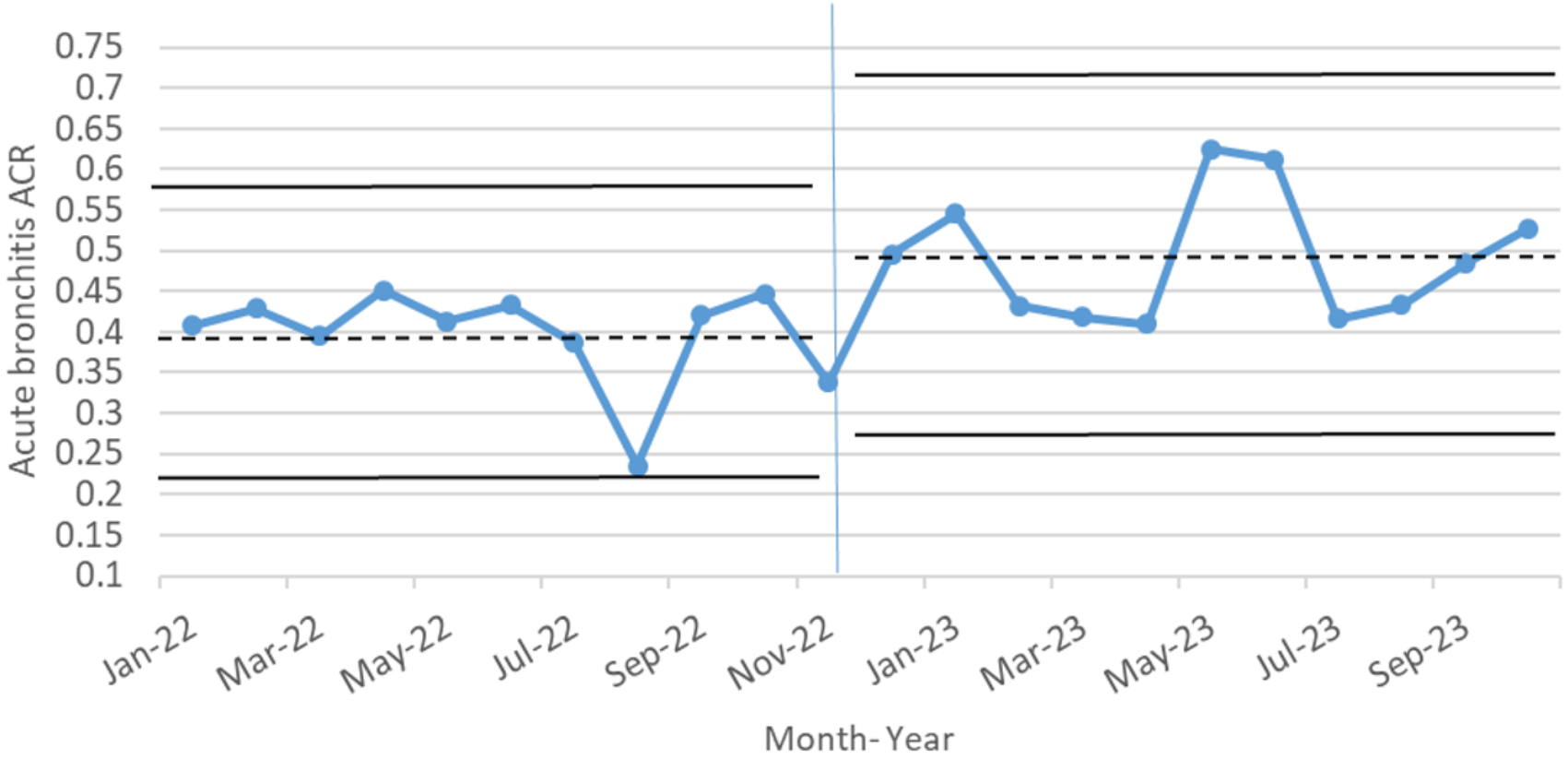
SECONDARY OUTCOMES

Appropriate care rates for upper respiratory tract infection antibiotic prescribing in the pre- and post-intervention periods by diagnosis.

Appropriate Care Rate	Pre-Intervention		Post-Intervention		t-test	p-value
	N	Mean (SD)	N	Mean (SD)		
AURI	179	0.82 (0.19)	172	0.85 (0.20)	-1.37	0.085
Bronchitis	151	0.39 (0.40)	139	0.49 (0.41)	-2.05	0.021
Pharyngitis	179	0.84 (0.20)	172	0.86 (0.20)	-0.71	0.239

Abbreviation: AURI, acute upper respiratory tract infection.

MIXED EFFECTS MODEL - BRONCHITIS



Abbreviations: ACR, appropriate care rate; Jan, January; Mar, March; Jul, July; Sep, September; Nov, November.

SECONDARY OUTCOMES (CONT.)

Mixed effects models for composite and bronchitis appropriate care rates for antibiotic prescribing by provider type.

ACR by Provider Type	β	Standard Error	Z	p-value	95% CI	
Composite	0.078	0.086	0.91	0.361	-0.090	0.246
Bronchitis	-0.137	1.008	-0.14	0.892	-2.114	1.839

DISCUSSION

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FINDINGS SUMMARY

- Primary outcome of composite ACR for acute upper respiratory infection, bronchitis, and pharyngitis without a positive Group A *Strep.* test showed statistically significant improvement after intervention
  - Mixed effects regression model showed the effect was consistent across all provider types
  - This result was consistent with the ACR for bronchitis
  - The individual ACRs for acute upper respiratory tract infection and pharyngitis did not show statistical significance but trended toward improvement

LIMITATIONS

- Data collection via an electronic algorithm
  - Removes the ability to assess patient-specific factors outside of ICD-10-CM codes
- Timeframe of current data collection only includes two groups of interventions (i.e., two rounds of report cards and two educational meetings)
  - Unable to assess how the efficacy of this intervention withstands over time

CONCLUSION

In this single-center, longitudinal, pre-post study, recurrent individualized feedback paired with provider education was associated with an improvement in appropriate antibiotic prescribing for upper RTIs in the urgent care setting.

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- Research Mentors:
  - Maxx Enzmann, PharmD, BCPS, BCIDP
  - Dubert Guerrero, MD, DTM&H, FIDSA
  - Leslie Laam, PhD

POST-ASSESSMENT QUESTION

True or False: Antibiotics are always indicated for acute upper respiratory tract infections.

False

QUESTIONS

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REFERENCES

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The Joint Commission. Accessed August 28, 2023. https://www.jointcommission.org/

Schwartz KL, Ivers N, Langford BJ, et al. Effect of Antibiotic-Prescribing Feedback to High-Volume Primary Care Physicians on Number of Antibiotic Prescriptions: A Randomized Clinical Trial. *JAMA Int Med*. 2021;181(9):1165-1173.

Dutcher L, Degnan K, Adu-Gyamfi AB, et al. Improving Outpatient Antibiotic Prescribing for Respiratory Tract Infections in Primary Care: A Stepped-Wedge Cluster Randomized Trial. *Clin Infect Dis*. 2022;74(6):947-956.

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Early Use Milrinone for Vasospasm Prevention in Aneurysmal Subarachnoid Hemorrhage

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Disclosures

- The speaker has no actual or potential conflict of interest in relation to this presentation.

United States' largest not-for-profit rural healthcare system

Sanford Health includes:
46 medical centers
210 clinic locations
208 senior living communities
158 skilled nursing and rehab facilities

Centers of Excellence:
Cancer
Children's
Heart
Orthopedics/Sports Medicine
Women's Health

Each year provides:
5.5 million outpatient and clinic visits
212,077 emergency department visits
88,368 admissions
140,510 surgeries and procedures
9,602 births

Learning objective

- Discuss the potential for use of early milrinone in patients with aneurysmal subarachnoid hemorrhage (aSAH) to improve patient outcomes

Pre-assessment Question

- Preventing vasospasm in patients after aneurysmal subarachnoid hemorrhage (SAH) is primarily done to prevent which adverse outcome?
  A. Delayed cerebral ischemia
  B. Hypertension
  C. Recurrence of hemorrhage
  D. Hypotension

Background

Background

- Severity of hemorrhage based on Fisher grade (1-4)
- aSAH is associated with high mortality rates
  - Increased risk in higher Fisher grades

Fisher Grade	
1	No haemorrhage evident
2	Subarachnoid haemorrhage < 1mm thick
3	Subarachnoid haemorrhage > 1mm thick
4	Subarachnoid haemorrhage of any thickness with intraventricular haemorrhage or parenchymal extension

Image from:
https://epos.myesr.org/posterimage/esr/ranzcr2011/108472/mediagallery/376803

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Background

Delayed cerebral ischemia (DCI) is the most prevalent reason for increased mortality

- Most often caused by vasospasm
- Patients with higher Fisher score are more likely to experience more severe vasospasm

Vasodilatory effects of milrinone potentially beneficial in vasospasm prevention

- Data is limited

Existing Literature

- Montreal Protocol (2012)
  - Case series using milrinone for treating vasospasm with a change in neurological status (n=88)
  - 49% able to go back to previous neuro baseline
  - 75% had good functional outcome (modified Rankin scale $\leq$ 2)
- MILRISPASM Trial (2021)
  - Controlled observational study (n=94)
  - Compared milrinone with induced hypertension versus induced hypertension alone
  - Association of lower 6-month functional disability and vasospasm-related infarction with milrinone
  - Endovascular angioplasty less frequent in milrinone group

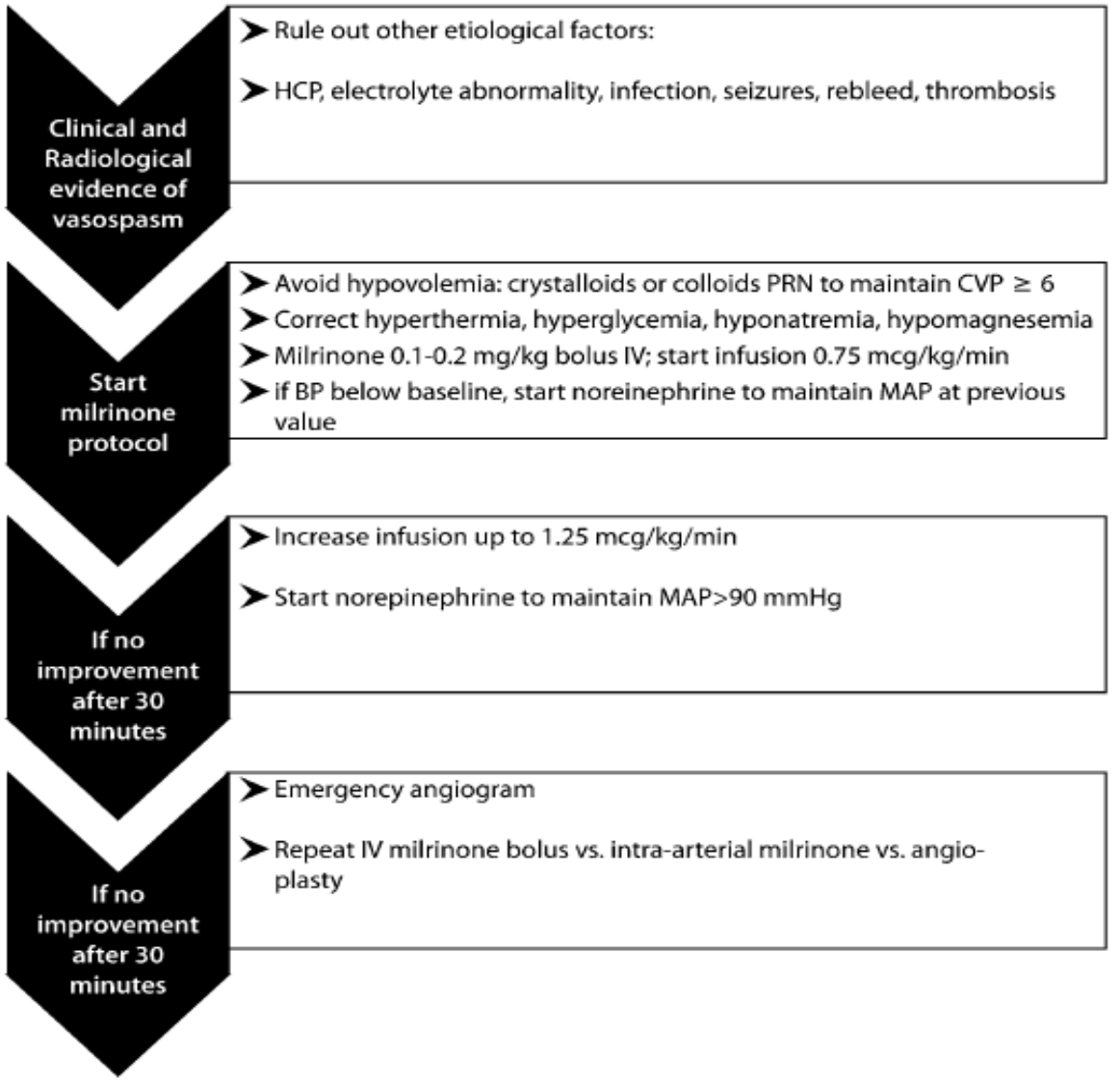

Image from: Lannes M, *Neurocrit Care,* 2012

Lakhal K, *Neurocrit Care*, 2021
Lannes M, *Neurocrit Care,* 2012

Study Objective

Assess the early use of milrinone after detection of vasospasm for reducing the incidence of delayed cerebral ischemia secondary to aSAH

Methods

Study Design

- Single center, retrospective, propensity-matched cohort study of patients aged 18 years or older admitted to Sanford Medical Center Fargo for aneurysmal SAH with Fisher score 3-4, initiated on nimodipine, between August 2016 and January 2024
- Daily transcranial dopplers (TCD) utilized for identification of vasospasm

Treatment groups:

- Intervention: Use of early milrinone upon identification of moderate to severe vasospasm on TCD
- Control: Standard of care for vasospasm treatment
- Groups were matched 1:2 based on age, sex, and fisher score

Outcomes

Primary outcome: Confirmed presence of DCI on imaging and increase of 4 points in the National Institute of Health Stroke Scale

Outcomes

Secondary outcomes:

- Occurrence of endovascular intervention due to vasospasm
- Hospital and ICU lengths of stay
- Location of discharge

Adverse outcomes:

- Myocardial ischemia
- Arrhythmia
- Hyponatremia
- Hypokalemia
- Incidence of hypotension

Results

Population - Baseline Characteristics

Characteristic	Milrinone (n=24)	Control (n=48)	P-value
Age (years)[b]	56 (43.3-66)	56 (48-65)	0.77
Male sex [a]	7 (29%)	18 (37%)	0.48
Weight, kg [b]	78.3 (63.7-89.7)	84.5 (69.9-98)	0.20
Diabetes[a]	2 (8%)	3 (6%)	1
Hypertension[a]	14 (58%)	20 (41%)	0.18
ASCVD[a]	1 (4%)	3 (6%)	1
CVA history[a]	1 (4%)	4 (8%)	0.65
Smoking status [a] **Current** **Previous** **Never**	 13 (54%) 5 (21%) 6 (25%)	 22 (46%) 8 (17%) 18 (37%)	0.56
Admit hydrocephalus [a]	13 (54%)	28 (58%)	0.73
Admit glucose, mg/dL [b]	135 (121-155)	149 (125-171)	0.27
Admit sodium, mEq/L [b]	140 (138-142)	139 (137-140)	0.16
Admit magnesium, mEq/L [b]	1.9 (1.6-2)	1.8 (1.7-1.9)	0.56

*denotes number (IQR); [a] denotes number (%); [b] denotes median (IQR)

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Baseline Characteristics Continued

Characteristic	Milrinone (n=24)	Control (n=48)	P-value
Fisher grade [a]			0.72
3	8 (33%)	18 (38%)	
4	16 (66%)	30 (62%)	
Aneurysm treatment method [a]			0.57
Clip	1 (4%)	5 (11%)	
Coil	21 (88%)	37 (77%)	
Stent	1 (4%)	5 (11%)	
Unsecured	1 (4%)	1 (2%)	
Time to initial moderate to severe vasospasm onset days, mean (± SD)	5.7 (3.17)	5.5 (2.61)	0.85
Highest severity of vasospasm [a]			0.21
Severe	10 (42%)	11 (23%)	
Moderate	8 (33%)	14 (29%)	
Mild	5 (21%)	16 (33%)	
None	1 (4%)	7 (15%)	
Repeat DSAs, mean (± SD)	2.25 (0.67)	2.3 (0.62)	0.56

*denotes number (IQR); [a] denotes number (%); [b] denotes median (IQR)

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Primary Outcome

	Milrinone (n=24)	Control (n=48)	P-value
Occurrence of confirmed DCI with increase of NIHSS by 4 [a]	12 (50%)	13 (27%)	0.0542

*denotes number (IQR); [a] denotes number (%); [b] denotes median (IQR)

Secondary Outcomes/Adverse Events

	Milrinone (n=24)	Control (n=48)	P-value
Intra-arterial catheter lab intervention [a]	10 (42%)	15 (31%)	0.56
ICU length of stay, days [b]	14.8 (12.9-18.6)	14.5 (12.7-16.9)	0.46
Hospital length of stay, days [b]	16.7 (14.3-20.8)	15.7 (13.4-19.6)	0.32
Discharge location [a] **Home** **Home health** **Rehab** **Nursing home** **Hospice/expired**	 6 (25%) 2 (8%) 12 (50%) 3 (13%) 1 (4%)	 19 (40%) 2 (4%) 20 (42%) 0 7 (14%)	0.054
Hypotension [a]	2 (8%)	5 (10%)	1
Cardiomyopathy [a]	0	2 (4%)	0.54
Arrhythmia [a]	3 (12%)	7 (14%)	1
Hypoglycemia [a]	0	0	---
Hypokalemia [a]	11 (46%)	9 (19%)	0.01
Hyponatremia [a]	15 (62%)	23 (48%)	0.24

*denotes number (IQR); [a] denotes number (%); [b] denotes median (IQR)

Discussion

Findings Summary

No significant difference was found in the occurrence of DCI with change in neurological status with early use of milrinone after detection of vasospasm

No significant difference in secondary outcomes

Significantly higher incidence of hypokalemia in milrinone group

Limitations

Retrospective data analysis

- Patient identification through nimodipine use may have led to missing patients if patients did not have nimodipine ordered due to allergy or hypotension
- Documentation of multiple patient factors such as NIHSS scoring inconsistent
- Discharge location used as surrogate for neurologic function on discharge due to under-utilization of modified Rankin scale
- Evolving practice in cares for aSAH during time-period of data collection

Dosing of milrinone not standardized across patients

Conclusions

In this single-center retrospective analysis, there was no association found with use of early milrinone and decreased occurrence of DCI with improved neurological outcomes with a trend toward worsened overall outcomes

Patients in the milrinone group had more severe baseline characteristics with higher rates of severe vasospasm, yet no significant difference in discharge location was found

Acknowledgments

- Research Mentors:
  - Jodi Atterberg, PharmD, BCCCP
  - Megan Moore, PharmD, BCPS, BCCCP
  - Qasim Durrani, MD

Post-assessment Question

- Preventing vasospasm in patients after aneurysmal subarachnoid hemorrhage (SAH) is primarily done to prevent which adverse outcome?
  A. Delayed cerebral ischemia
  B. Hypertension
  C. Recurrence of hemorrhage
  D. Hypotension

Questions?

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Phenylephrine vs. Norepinephrine in ICU Shock Patients in Atrial Fibrillation with Rapid Ventricular Rate

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Disclosures

The speaker has no actual or potential conflict of interest in relation to this presentation.

United States' largest not-for-profit rural healthcare system

Sanford Health includes:
46 medical centers
210 clinic locations
208 senior living communities
158 skilled nursing and rehab facilities

Centers of Excellence:
Cancer
Children's
Heart
Orthopedics/Sports Medicine
Women's Health

Each year provides:
5.5 million outpatient and clinic visits
212,077 emergency department visits
88,368 admissions
140,510 surgeries and procedures
9,602 births

Learning Objective

- Assess the heart rate and rhythm effects of intensive care unit patients in atrial fibrillation with rapid ventricular rate treated with norepinephrine or phenylephrine

Pre-assessment question

Which of the following is true when comparing the adrenergic stimulation of norepinephrine to phenylephrine?

- A. Phenylephrine has beta activity that may stimulate an increase in heart rate
- B. Norepinephrine has beta activity that may stimulate an increase in heart rate
- C. Phenylephrine has alpha activity that may directly stimulate an increase in heart rate
- D. Norepinephrine has alpha activity that may directly stimulate an increase in heart rate

Background

Atrial Fibrillation

Common in the ICU: 15-25%

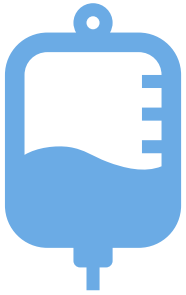
Associated with increased hospital mortality

Rapid ventricular rate (RVR)= heart rate ≥ 110

Causes hemodynamic instability with decreased ventricular filling time

Wetterslev. Critical Care Medicine. 2023
Shaver. Critical Care Medicine. 2023

Shock



0xygen perfusion ≠ tissue demands

Life-threatening circulatory failure

Cardiogenic

Distributive

Hypovolemic

Obstructive

Evans. Critical Care Medicine. 2021

Vasopressors

	Norepinephrine	Phenylephrine
Mechanism of Action	↑↑↑ α-1 : ↑ β-1	↑↑↑↑ α-1
Dosing	Wt-based: 0.01-3 mcg/kg/min Non-wt-based: 80-250 mcg/min	Wt-based: 0.4-9.1 mcg/kg/min Non-wt-based: 20-400 mcg/min
Side Effects	Tachycardia	Bradycardia
Conversion	Phenylephrine x 0.06 = Norepinephrine (mcg/kg/min)	

Receptor	Effect	Agents
α-1	↑vasoconstriction=↑SVR	Phenylephrine
β-1	↑contractility and heart rate	Norepinephrine

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Overgaard. Circulation. 2008
Kotani. Crit Care. 2023

Mortality in Patients Treated with Phenylephrine in Septic Shock

Is there a mortality difference in patients treated with phenylephrine for septic shock?

Retrospective, chart review.

Phenylephrine vs. no phenylephrine in patients with septic shock in the ICU.

n= 148 vs. 321

<u>Primary outcome: 90-day mortality</u>
Phenylephrine: 56%
Non-phenylephrine: 41%
p=0.003

<u>Tachycardia: 90-day mortality</u>
Phenylephrine: 54%
Non-phenylephrine: 36%
p=0.02

Utilization of phenylephrine in septic shock patients, especially those with ongoing tachycardia, was associated with an increased rate of mortality

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Patel et al. Journal of Pharmacy Practice. 2021

Time to Rate Control in Patients Switched from Phenylephrine to Norepinephrine

Is there a rate control difference in Afib with RVR patients with septic shock treated with norepinephrine vs. transition to phenylephrine?

Retrospective, cohort, chart review.

Transitioned from norepinephrine to phenylephrine vs. remained on norepinephrine

n= 28 vs. 39

<u>Time to Rate Control (unadjusted):</u>
HR 1.99 (95% CI: [1.19-3.34] p<0.01)

<u>Time to Rate Control (adjusted):</u>
HR 1.75 (95% CI: [0.86-3.53] p=0.12)

<u>30-day mortality</u>
Norepinephrine: 61%
Phenylephrine: 71%
p=0.4

Potential clinical effect on achieving rate control cannot be excluded. Unclear if there is a benefit on mortality or length of stay.

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Haiduc. Journal of Intensive Care Medicine. 2021

Heart Rate after Phenylephrine vs Norepinephrine Initiation

Among patients with sepsis and atrial fibrillation, what is the difference in heart rate after phenylephrine vs. Norepinephrine initiation?

Retrospective, cohort, chart review.

HRs at hours 1 and 6 in norepinephrine vs. phenylephrine patients with septic shock and Afib in the ICU.
n= 946 vs. 901

Primary outcome: Heart Rate Difference
1 hour: -4 bpm (95% CI: [-6 to –1] p<0.001)
6 hour: -4 bpm (95% CI: [-6 to –1] p=0.004)

Subgroup With RVR
1 hour: -4 bpm (95% CI: [-9 to 0] p=0.049)
6 hour: -6 bpm (95% CI: [-11 to –1] p=0.02)

Initiation of phenylephrine was associated with modestly lower heart rate compared with norepinephrine. Heart rate at vasopressor initiation appeared to be an important effect modifier.

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Law et al. CHEST. 2022

Study Objective

To compare the rate and rhythm of critically ill patients in atrial fibrillation with rapid ventricular rate treated with norepinephrine or phenylephrine at hours 6 and 24

Methods

Study Design

Single-Center Retrospective Cohort

- Sanford Medical Center Fargo (Fargo, ND)

EPIC Slicer Dicer

- Atrial Fibrillation + Shock Diagnosis
- SNOMED Diagnosis of Atrial Fibrillation with Rapid Ventricular Rate
- August 2018 – December 2023

Cohorts

- Phenylephrine vs. Norepinephrine

Criteria

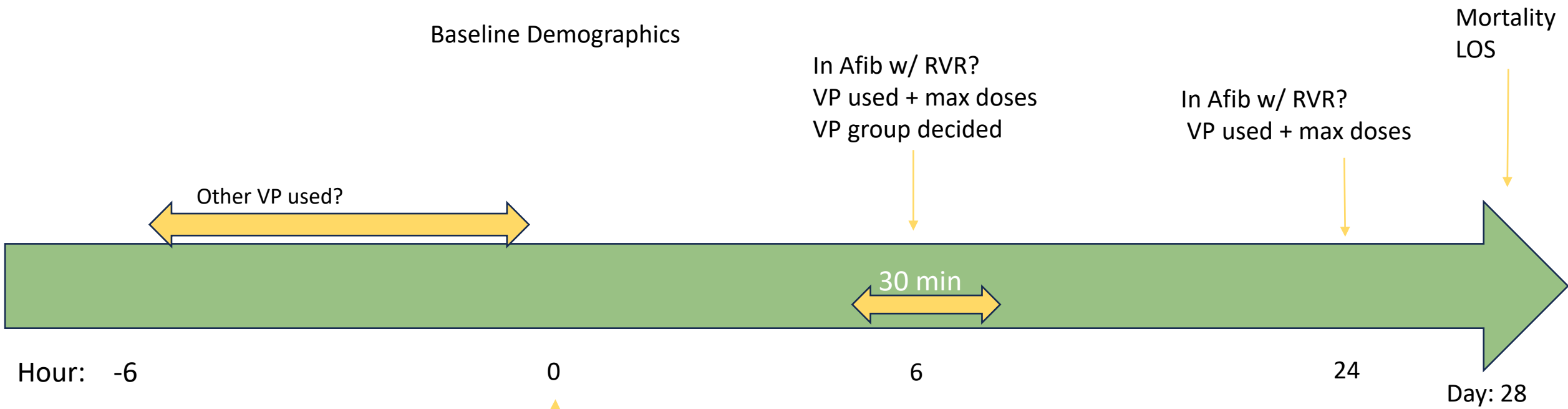
Inclusion Criteria

- ≥18 years old
- Admission to medical, surgical or neurological ICU
- Ongoing vasopressor titration with phenylephrine or norepinephrine through hour 6 for the treatment of shock
- Atrial fibrillation with rapid ventricular rate (BPM ≥110) at hour 0

Exclusion Criteria

- Cardiothoracic surgery admission

Timeline


Baseline Demographics
In Afib w/ RVR?
VP used + max doses
VP group decided
In Afib w/ RVR?
VP used + max doses
Mortality
LOS
Other VP used?
30 min
Hour: -6
0
6
24
Day: 28
Vasopressor initiation
+
Afib w/ RVR

Outcomes

Primary Outcome

- Incidence of Atrial Fibrillation with Rapid Ventricular Rate at Hour 24

Secondary Outcomes

- Incidence of Atrial Fibrillation with Rapid Ventricular Rate at Hour 6
- In-Hospital 28-day Mortality
- Hospital Length of Stay
- ICU Length of Stay

Results

Demographics

	Norepinephrine (n=104)	Phenylephrine (n=36)
Male, N (%)	67 (64.4)	24 (66.7)
Weight – median, Kg	87.5 [69.85-106.48]*	89.7 [66.8-100.75]
Age – median, years	72.5 [66.25-79.75]*	73.5 [66.75-79.75]*
CHF history, N (%)	55 (52.88)	15 (41.67)
Afib history, N (%)	62 (59.62)	18 (50.00)
SMS-ICU	23 [20-27.5]*	23.5 [20-25]*
Shock		
Distributive, N (%)	73 (70.19)	28 (77.78)
Cardiogenic, N (%)	16 (15.38)	2 (5.6)
Hypovolemic, N (%)	6 (5.7)	3 (8.3)
Neurogenic, N (%)	1 (1)	1 (2.8)
Obstructive, N (%)	0	0
Combined, N (%)	8 (7.6)	2 (5.6)

*= Interquartile ranges

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ICU Admission Type

	Norepinephrine (n=104)	Phenylephrine (n=36)
Medical ICU, N (%)	84 (80.77)	28 (77.78)
Surgical ICU, N (%)	17 (16.35)	3 (8.33)
Neuro ICU, N (%)	2 (1.92)	5 (13.89)

Home Medications

	Norepinephrine (n=104)	Phenylephrine (n=36)	P-value
Any Rate or Rhythm Agent, N (%)	65 (62.5)	21 (58.33)	0.66
Beta-blocker, N (%)	58 (55.7)	15 (41.7)	0.42
Calcium Channel Blocker, N (%)	8 (7.7)	6 (16.7)	0.12
Antiarrythmic, N (%)	13 (12.5)	4 (11.1)	0.82
Digoxin, N (%)	11 (10.6)	6 (2.78)	0.15

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Hospital Administered Medications (0-24 hours)

	Norepinephrine (n=104)	Phenylephrine (n=36)	P-value
Any Rate or Rhythm Agent, N (%)	88 (84.62)	29 (80.56)	0.57
Beta-blocker, N (%)	17 (16.35)	11 (30.56)	0.07
Calcium Channel Blocker, N (%)	5 (4.81)	2 (5.56)	0.86
Antiarrythmic, N (%)	83 (79.81)	24 (66.7)	0.11
Digoxin, N (%)	16 (15.38)	4 (11.11)	0.53

Total Vasopressor Doses in NEE

	Norepinephrine (n=104)	Phenylephrine (n=36)	P-value
Hour -6	0.04 (0-0.18)	0.018 (0-0.09)	0.21
	NE: 0.025 (0-0.14)	NE: 0 (0-0)	<0.001
	PE: 0 (0-0)	PE: 0 (0-0.03)	<0.001
Hour 0	0.13 (0.06-0.3)	0.033 (0.026-0.113)	<0.0001
	NE: 0.12 (0.06-0.25)	NE: 0 (0-0.02)	<0.0001
	PE: 0 (0-0)	PE: 0.03 (0.012-0.06)	<0.0001
Hour 6	0.16 (0.07-0.32)	0.03 (0.024-0.12)	0.0001
	NE: 0.15 (0.07-0.28)	NE: 0 (0-0)	<0.0001
	PE: 0 (0-0)	PE: 0.03 (0.02-0.12)	<0.0001
Hour 24	0.09 (0.02-0.34)	0.03 (0-0.18)	0.11
	NE: 0.07 (0-0.24)	NE: 0 (0-0)	<0.0001
	PE: 0 (0-0)	PE: 0.02 (0-0.06)	<0.0001

All data expressed as medians with interquartile ranges

Heart Rate in beats per minute (0-24 hrs)

	Norepinephrine (n=104)	Phenylephrine (n=36)	P-value
Hour 0, median	119 (113-127.5)*	121 (112.5-130.75)*	0.6192
Hour 6, median	106 (91-120.75)*	101 (89.5-113)*	0.185
Hour 24, median	99.5 (82.25-112)*	102.5 (80-117.75)*	0.52

*= Interquartile ranges

Outcomes

	Norepinephrine (n=104)	Phenylephrine (n=36)	P-value
Primary			
Afib with RVR at hour 24, N (%)	30 (28.9)	14 (38.9)	0.26
Secondary			
Afib with RVR at hour 6, N (%)	42 (40.4)	12 (33.3)	0.45
Hospital (Days)	11.9 (7.7-16.7)*	11.5 (7.3-21.3)*	0.44
ICU (Days)	6.5 (3.6-11.7)*	7.0 (4.2-12.2)*	0.55
In-Hospital 28-day mortality, N (%)	63 (60.6%)	21 (58.3%)	0.81

*= Interquartile ranges

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Discussion

Limitations

- Retrospective study design
- Small sample size
- Population imbalance
- Single center

Conclusions

In ICU shock patients with atrial fibrillation and having a rapid ventricular rate, no significant composite rate and rhythm differences were seen at extended time points in patients treated with phenylephrine versus norepinephrine.

Post-assessment question

Which of the following is true when comparing the adrenergic stimulation of norepinephrine to phenylephrine?

- A. Phenylephrine has beta activity that may stimulate an increase in heart rate
- B. Norepinephrine has beta activity that may stimulate an increase in heart rate
- C. Phenylephrine has alpha activity that may directly stimulate an increase in heart rate
- D. Norepinephrine has alpha activity that may directly stimulate an increase in heart rate

Acknowledgments

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Questions?

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Thank you!

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