Rational Vasopressor Selection

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Disclosures

I have financial relationship(s) with:

Grant / Research:

PCORI – Co-investigator, "Trajectories of Recovery after Intravenous Propofol vs. Inhaled Volatile Anesthesia (THRIVE)" PI: Kheterpal/Avidan

Grant / Research (current):

NIH R01 – Co-investigator, 1R01LM01389401 "A scalable service to improve health care quality through precision audit and feedback" PI: Landis-Lewis

NIH R01 - Co-investigator, 1R01DK13322601 "Cardiac sURgery anesthesia Best practices to reduce Acute Kidney Injury (CURB-AKI) PI: Mathis/Singh

Grant / Research:

NIH T32 Research Fellowship Grant – 5T32GM103730-07 (past)

Grant / Research:

Becton Dickinson and Company (past)

Learning Objectives

- Recall vasopressor pharmacology and physiology
- Critically evaluate the literature surrounding vasopressor selection
- Apply the evidence supporting use of various vasopressors to daily clinical practice

Vasopressors

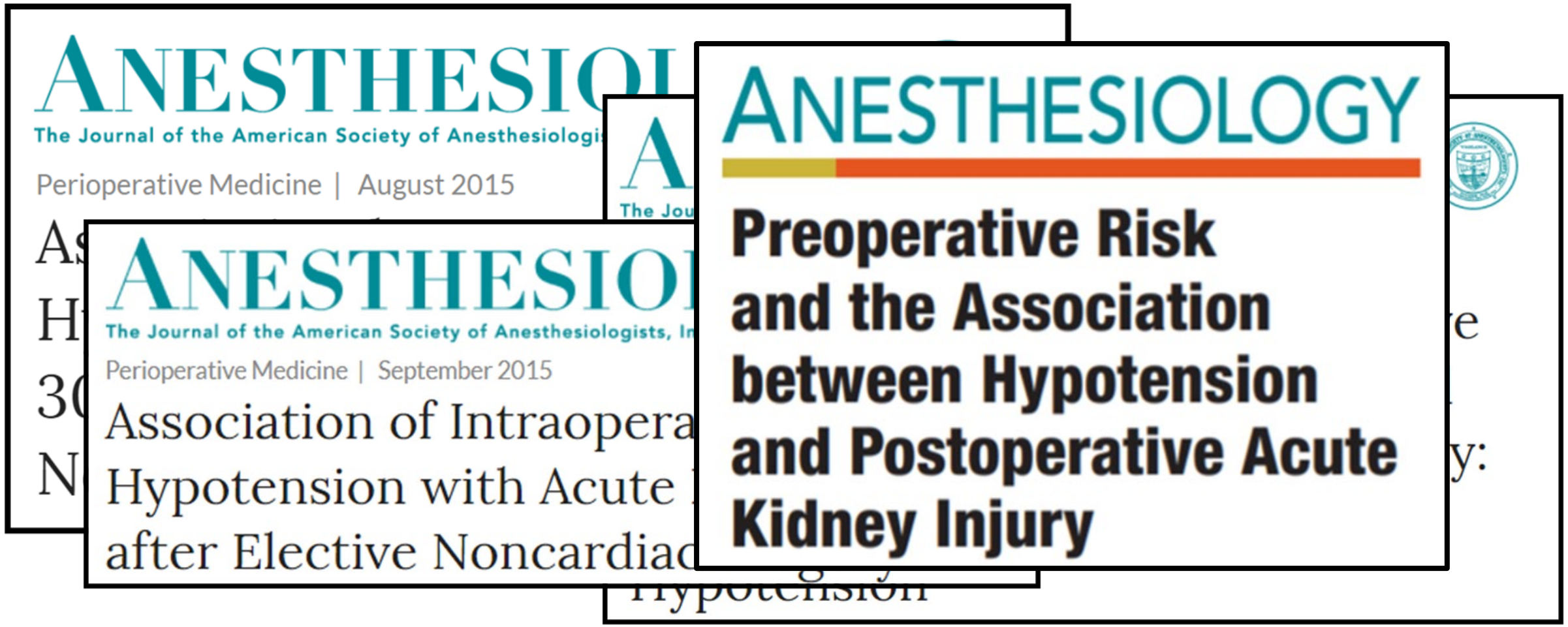
- Phenylephrine
- Ephedrine
- Vasopressin
- Dilute norepinephrine
- Concentrated norepinephrine
- Epinephrine
- Dopamine
- Angiotensin II

Background

- End-organ dysfunction is a major issue for surgical patients significantly impacting quality of life, recovery after surgery, and cost of care [1-8]

- Improved outcomes while maintaining intraoperative blood pressures [1-7]
- Vasopressor therapies, specifically the choice between phenylephrine and norepinephrine, are debated [9-13]

Hypotension & Postoperative Outcomes [1-7]



Vasopressors

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Rational Selection? Or Selection by Default?

- What patient or surgical factors contribute to your choice of vasopressor?
- What vasopressor options are available at each of your operative sites?
- Are there challenges to obtaining or using various options?
- Do we even know what the “best” option is?
- Which options are safe via peripheral IVs?

Vasopressors

	Receptor					Physiologic Effect			
Drug	**α1**	**β1**	**β2**	**V1**	**D**	**Cardiac Output**	**Vascular Tone**	**Blood pressure**	**Heart Rate**
Phenylephrine	+++	0	0	0	0	↓	↑↑	↑↑	↓
Norepinephrine	+++	+	0	0	0	↔	↑↑	↑↑	↔
Vasopressin	0	0	0	++	0	↔	↑↑	↑↑	↔
Ephedrine	++	++	++	0	0	↑	↑↑	↑↑	↑
Dopamine									
Low	0	+	0	0	++	↑	↔	↔	↔
Med	+	++	0	0	++	↑	↑	↑	↑
High	++	++	0	0	++	↔	↑↑	↑↑	↑
Epinephrine	+++	+++	++	0	0	↑↑	↑	↑↑	↑↑

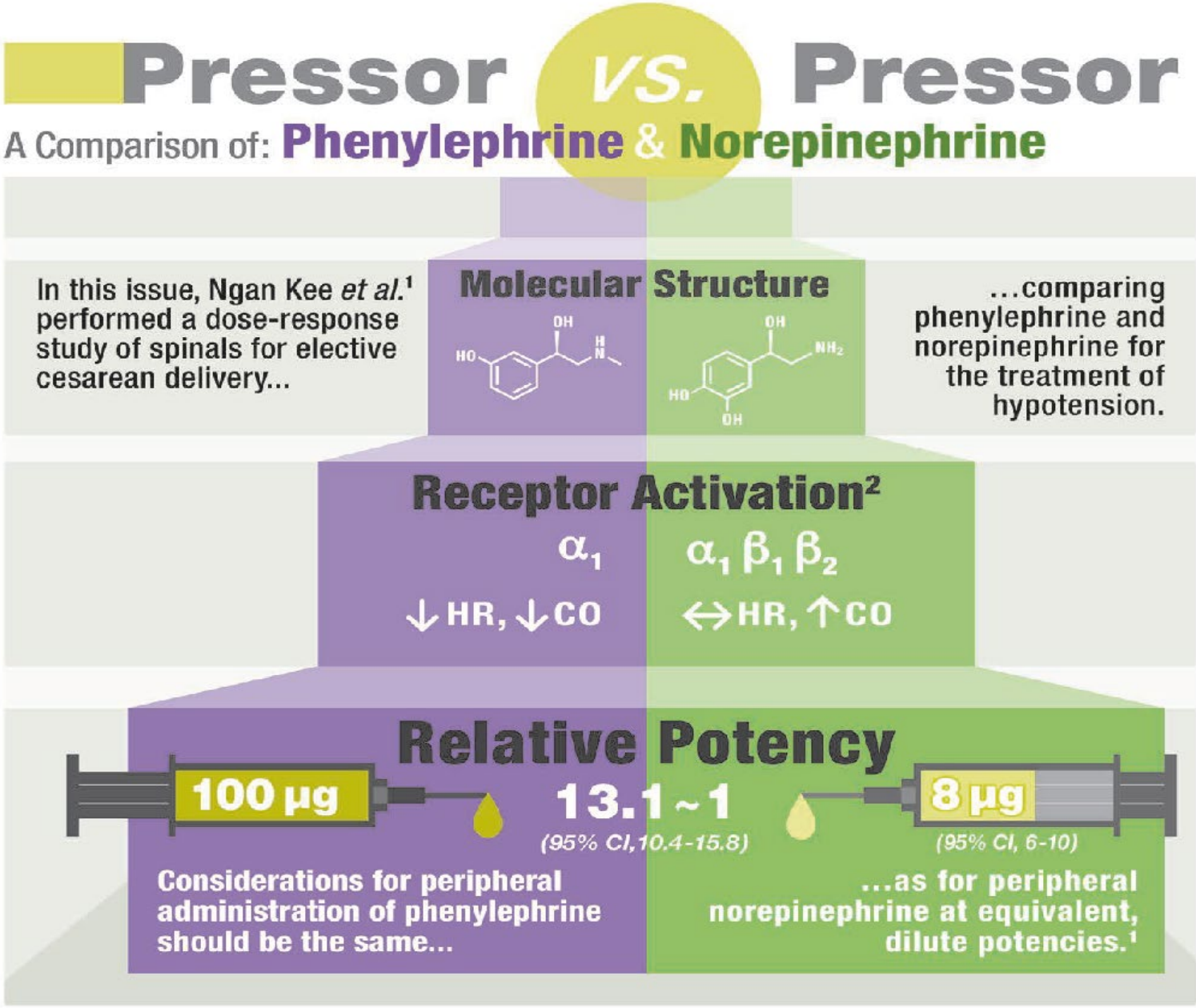
Dose Equivalency

The NEW ENGLAND JOURNAL of MEDICINE

Drug	Dose	Norepinephrine equivalent
Epinephrine[a]	0.1 μg/kg/min	0.1 μg/kg/min
Norepinephrine[a]	0.1 μg/kg/min	0.1 μg/kg/min
Dopamine[a]	15 μg/kg/min	0.1 μg/kg/min
Phenylephrine[b]	1.0 μg/kg/min	0.1 μg/kg/min
Vasopressin	0.04 U/min	0.1 μg/kg/min

[14] Khanna A, English SW, Wang XS, et al. Angiotensin II for the Treatment of Vasodilatory Shock. *The New England journal of medicine.* 2017;377(5):419-430

Dose Equivalency

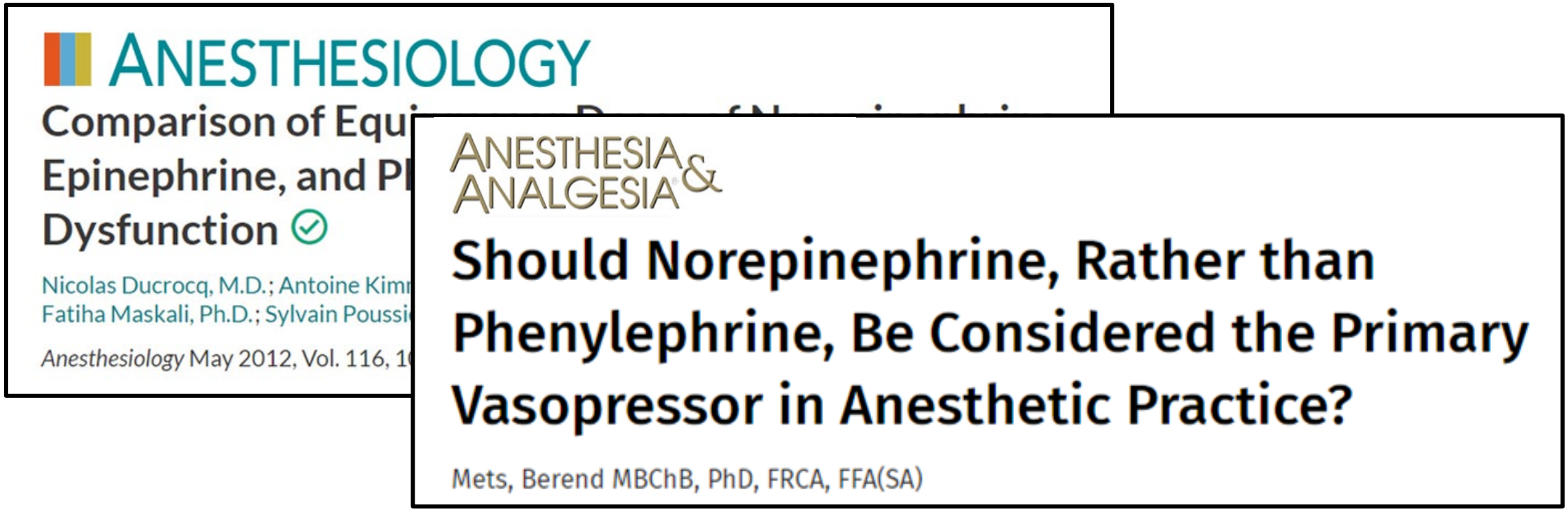


ANESTHESIOLOGY

Infographic created by Jonathan P. Wanderer, Vanderbilt University Medical Center, Anesthesiology, 2017 [15]

Literature - Phenylephrine and Norepinephrine

- Studies show norepinephrine is potentially superior to phenylephrine for some patient populations, given improved cardiac output [8-12]



Literature - Phenylephrine and Norepinephrine

- ICU patients: phenylephrine was associated with increased mortality during a norepinephrine drug shortage [10]

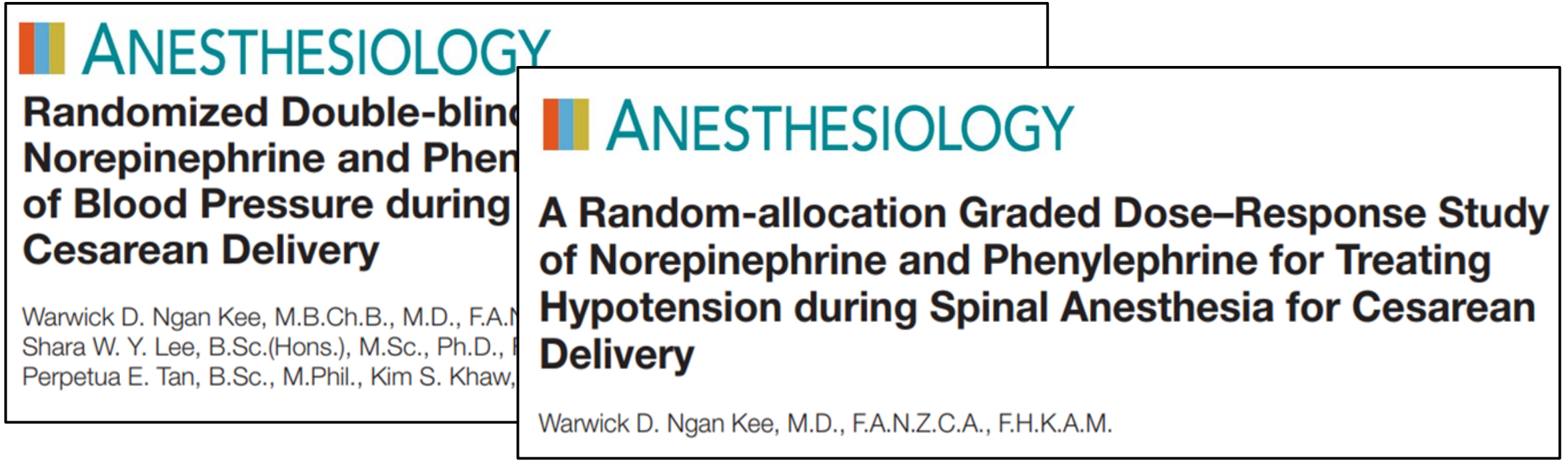
JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Association Between US Norepinephrine Shortage and Mortality Among Patients With Septic Shock

Emily Vail, MD; Hayley B. Gershengorn, MD; May Hua, MD, MSc; Allan J. Walkey, MD, MSc; Gordon Rubenfeld, MD, MSc; Hannah Wunsch, MD, MSc

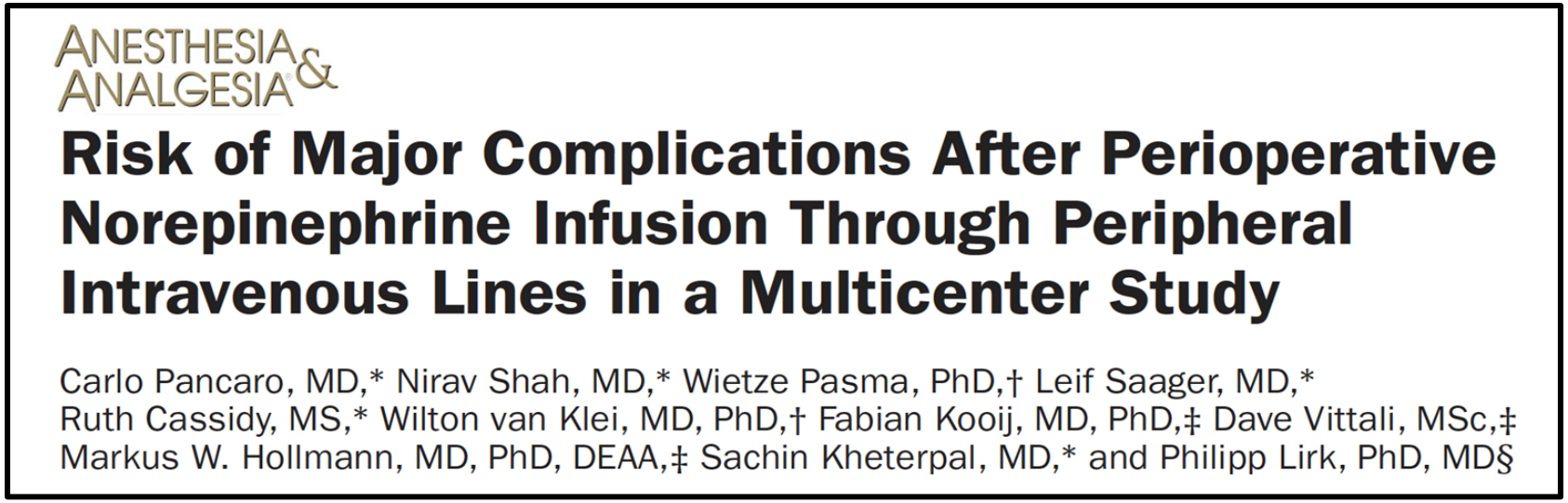
Literature - Phenylephrine and Norepinephrine

- OB patients: improved cardiac indices were found with norepinephrine compared to phenylephrine when used during cesarean section [12, 13]



New Safety Data - Dilute Norepinephrine

- No association between dilute peripheral norepinephrine infusions and complications due to peripheral IV extravasation or adverse events in >14,000 patients [16]
- Other studies also showed no increase in complications of IV extravasation with dilute peripheral norepinephrine [12, 13, 16-18]

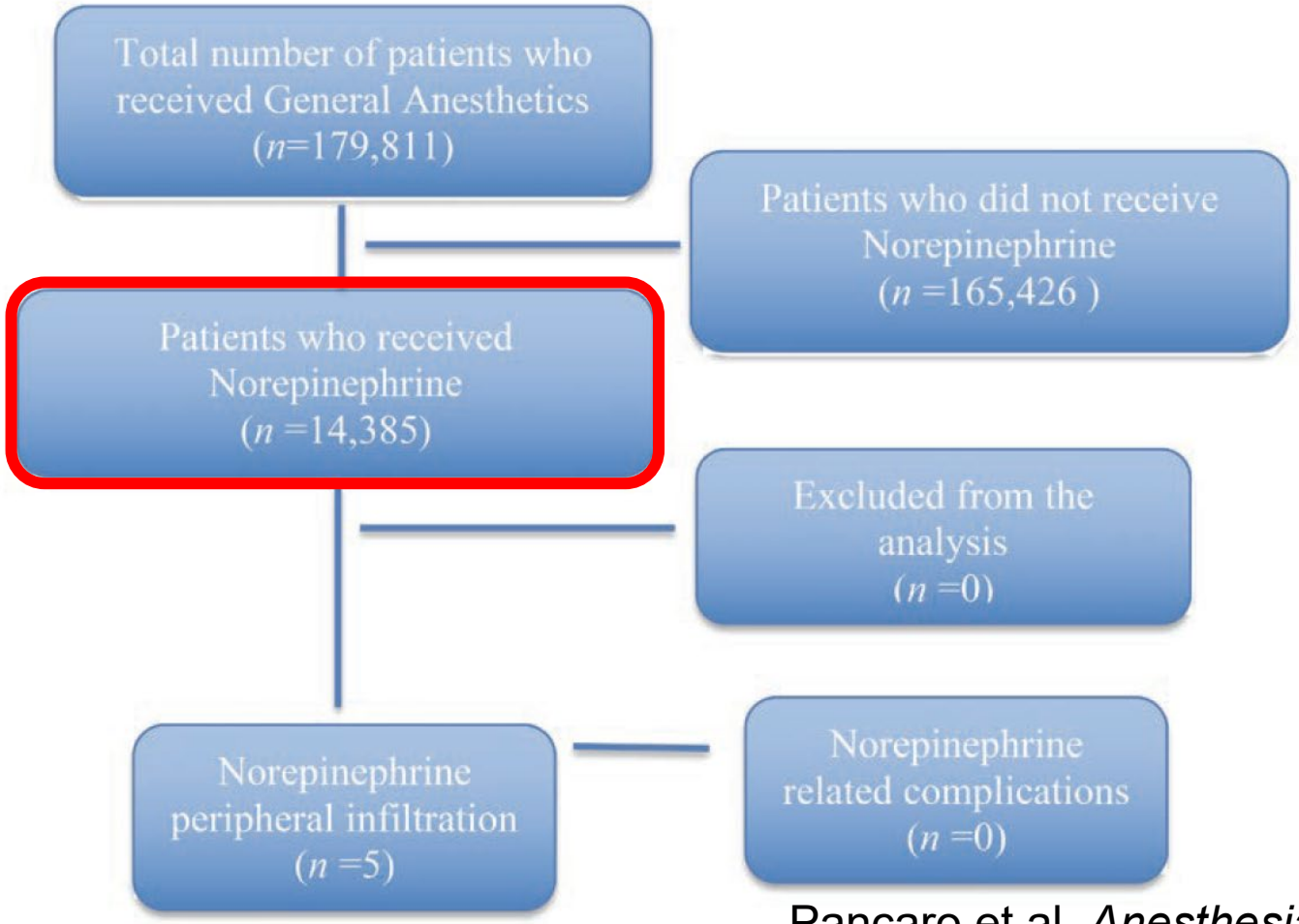


ANESTHESIA & ANALGESIA

Risk of Major Complications After Perioperative Norepinephrine Infusion Through Peripheral Intravenous Lines in a Multicenter Study

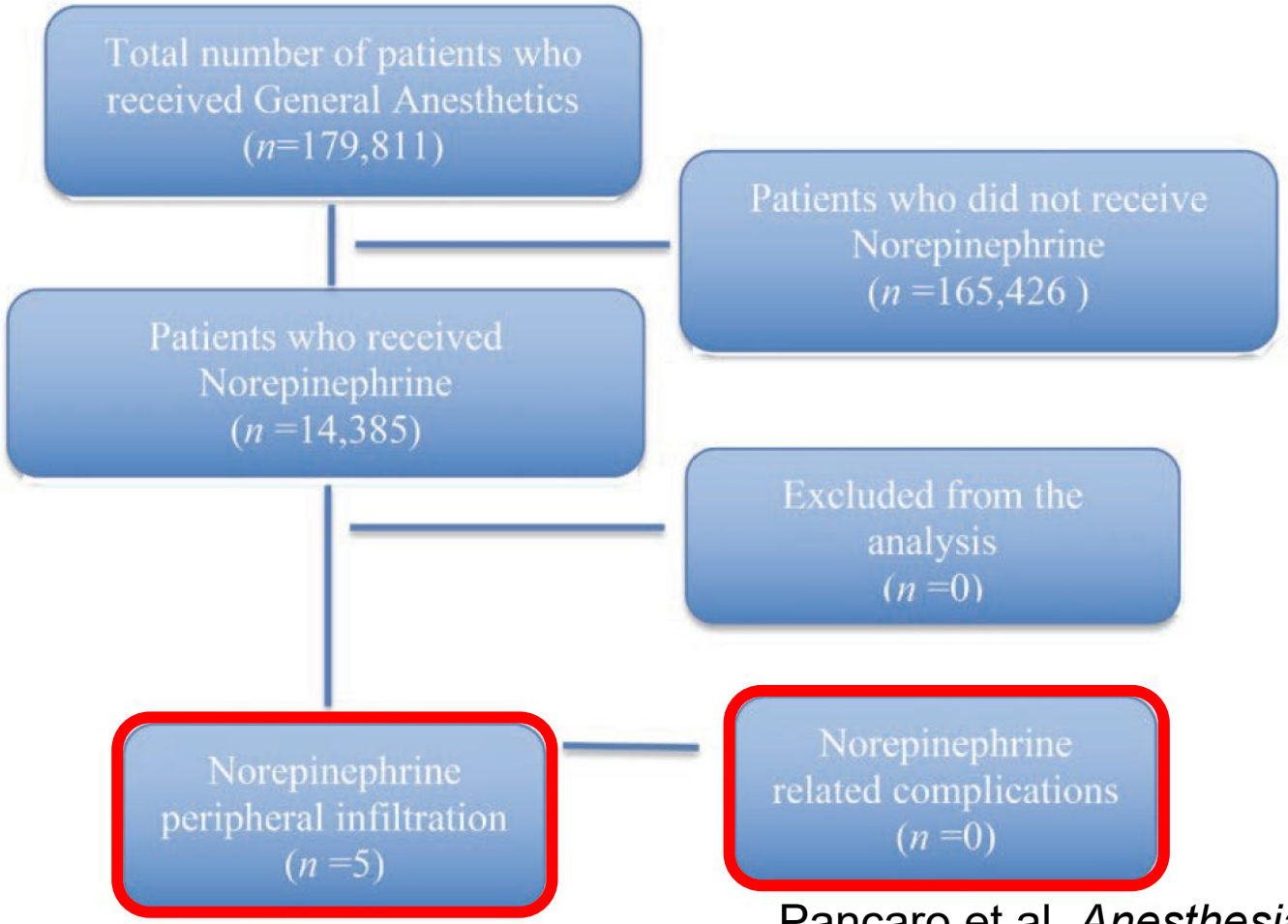
Carlo Pancaro, MD,* Nirav Shah, MD,* Wietze Pasma, PhD,† Leif Saager, MD,* Ruth Cassidy, MS,* Wilton van Klei, MD, PhD,† Fabian Kooij, MD, PhD,‡ Dave Vittali, MSc,‡ Markus W. Hollmann, MD, PhD, DEAA,‡ Sachin Kheterpal, MD,* and Philipp Lirk, PhD, MD§

New Safety Data - Dilute Norepinephrine



Pancaro et al, *Anesthesia and Analgesia*, 2019 [16]

New Safety Data - Dilute Norepinephrine



Pancaro et al, *Anesthesia and Analgesia*, 2019 [16]

New Safety Data - Dilute Norepinephrine

Zero Complications

Estimated risk of **0–2 adverse events per 10,000** patients
(95% CI of 0%–0.021%)

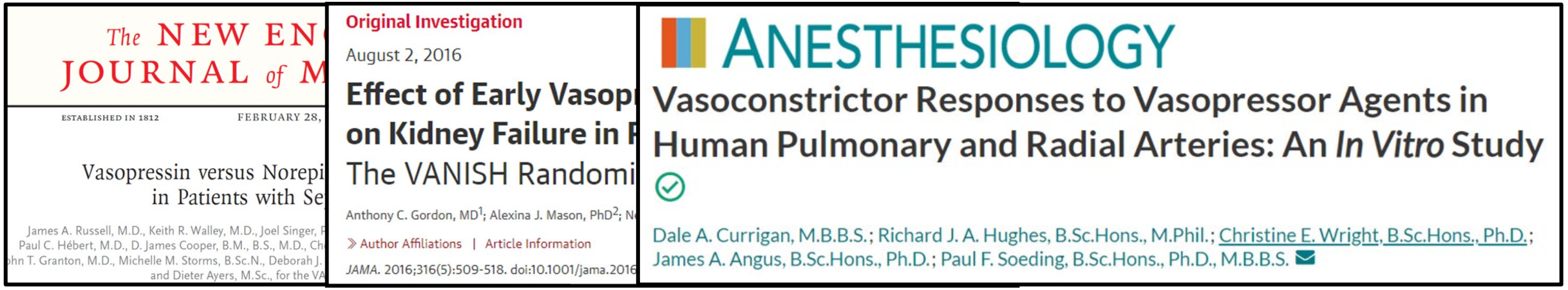
Pancaro et al, *Anesthesia and Analgesia*, 2019 [16]

Literature - Ephedrine

- A reduced the risk of postoperative organ dysfunction was found with norepinephrine compared to ephedrine, but this study is confounded by different blood pressure thresholds in each protocol [5]
- Ephedrine has been associated with worsened fetal acidosis compared to phenylephrine and norepinephrine [19,20]

Literature - Vasopressin

- Vasopressin can be used as an adjunct to norepinephrine for septic shock but does not improved mortality [21]
- In the VANISH trial, early use of vasopressin compared with norepinephrine did not improve the number of kidney failure–free days [22]
- Preferential vasoconstriction of the systemic circulation, sparing the pulmonary circulation, great choice for pulmonary hypertension [23]



Literature - Dopamine and Epinephrine

- For septic shock, dopamine is associated with greater mortality and a higher incidence of arrhythmic events compared to norepinephrine administration [24]
- Dopamine is able to be administered through a peripheral IV [25]
- Epinephrine for refractory hypotension or cardiac arrest

ORIGINAL ARTICLE

Comparison of Dopamine and Norepinephrine in the Treatment of Shock

Daniel De Backer, M.D., Ph.D., Patrick Biston, M.D., Jacques Devriendt, M.D., Christian Madl, M.D., Didier Chochrad, M.D., Cesar Aldecoa, M.D., Alexandre Brasseur, M.D., Pierre Defrance, M.D., Philippe Gottignies, M.D., and Jean-Louis Vincent, M.D., Ph.D. for the SOAP II Investigators*

Avoiding the 17-year lag[26]…

17 YEARS…

Rational Selection? Or Selection by Default?

- What patient or surgical factors contribute to your choice of vasopressor?
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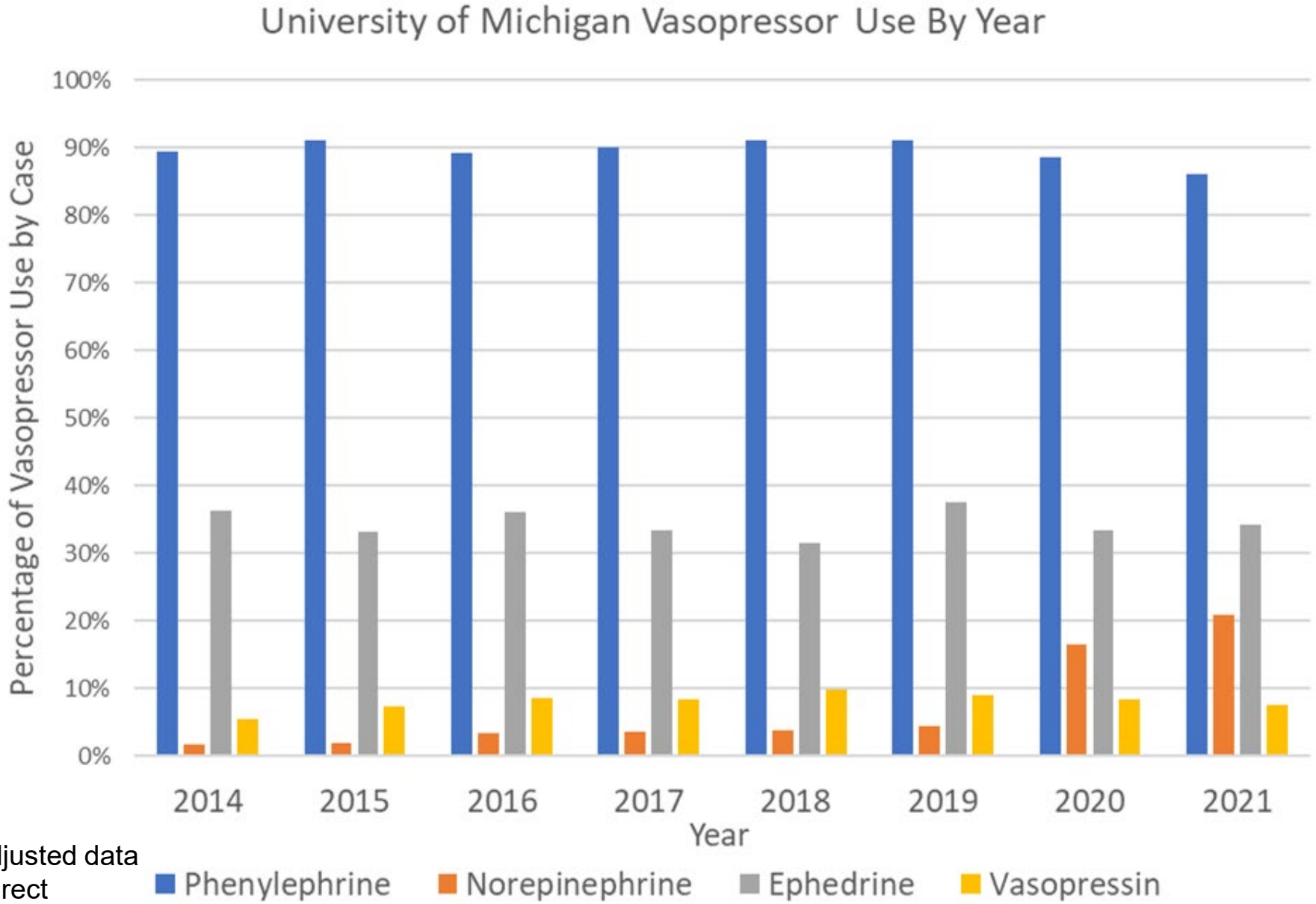
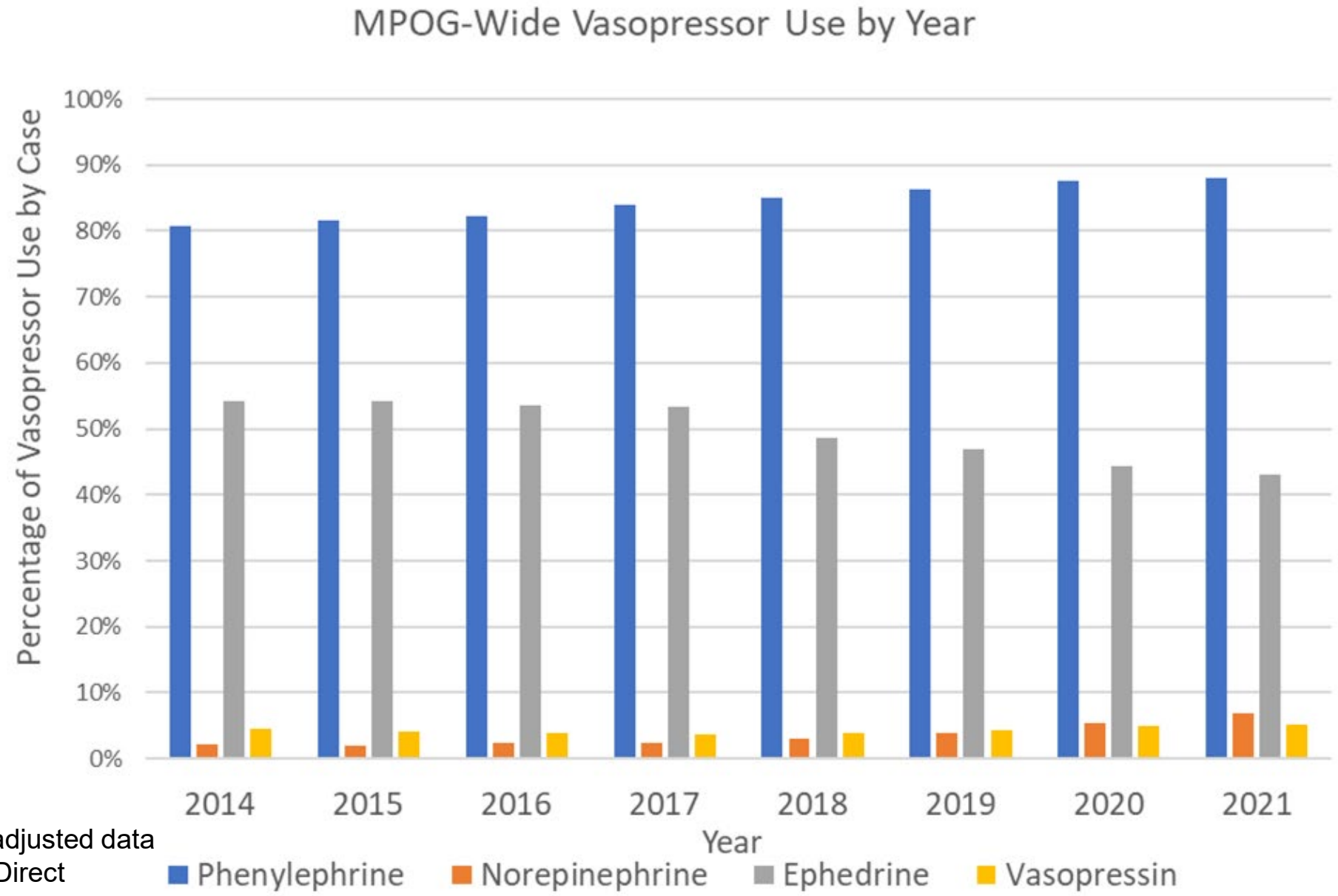


*Unpublished, unadjusted data from MPOG DataDirect

Changes in Patterns of Use at Michigan Medicine

- For non-cardiac cases without a central line, dilute norepinephrine use has increased over time:

Year	Dilute norepinephrine used in any case (%)	Dilute norepinephrine used in cases receiving any vasopressor (%)
2019	2.1%	3.8%
2020	9.8%	17.3%
2021	12.3%	21.4%



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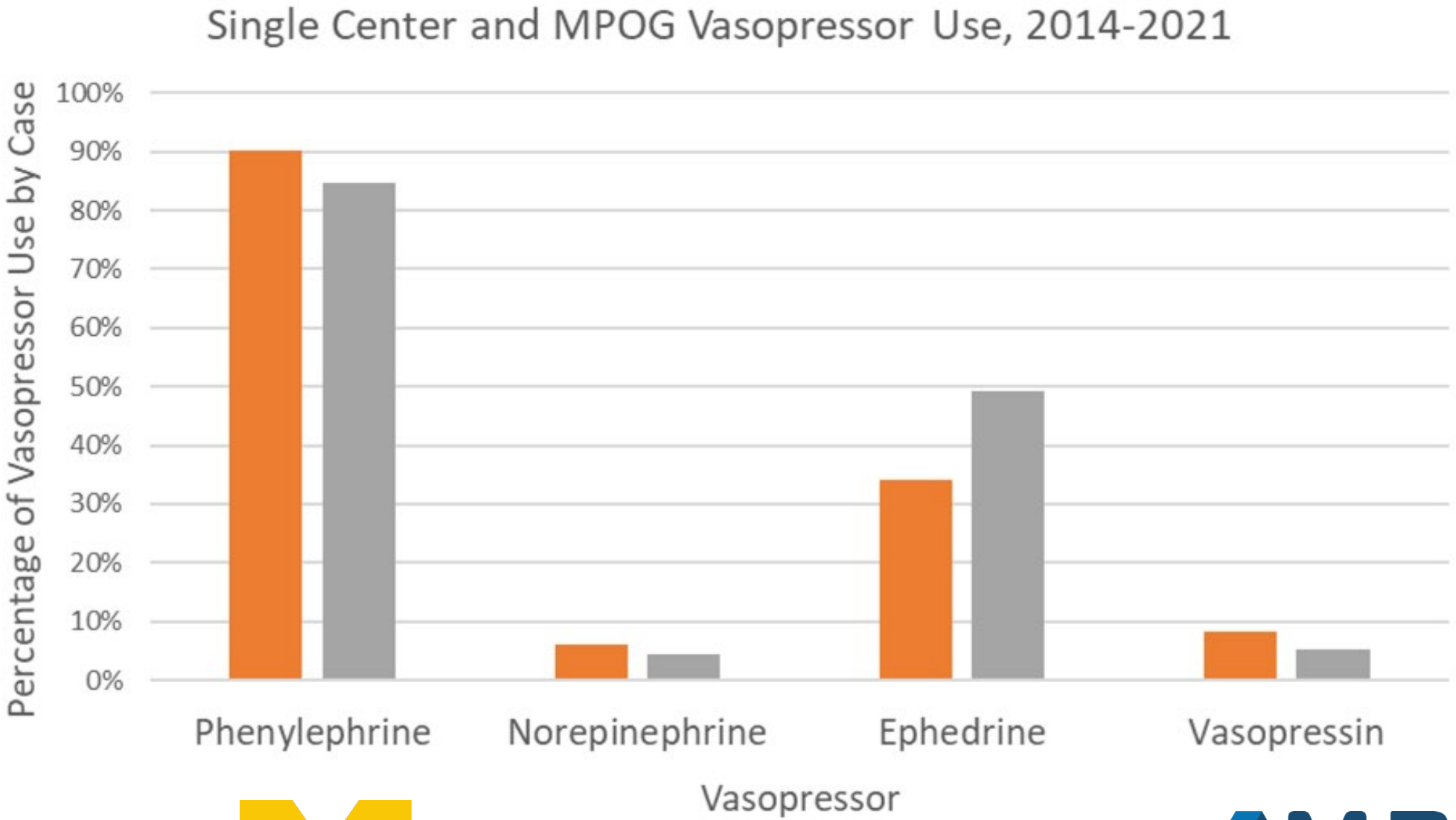

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MPOG MULTICENTER PERIOPERATIVE OUTCOMES GROUP

Road to Change

Approved Vasopressors at Michigan Medicine

- Phenylephrine (peripheral or central)
- Ephedrine (peripheral or central)
- Vasopressin (ideally central)
- Concentrated norepinephrine (central only)
- Dilute norepinephrine (peripheral or central)
- Epinephrine (ideally central)
- Angiotensin II (central only)

Approved Vasopressors at Michigan Medicine

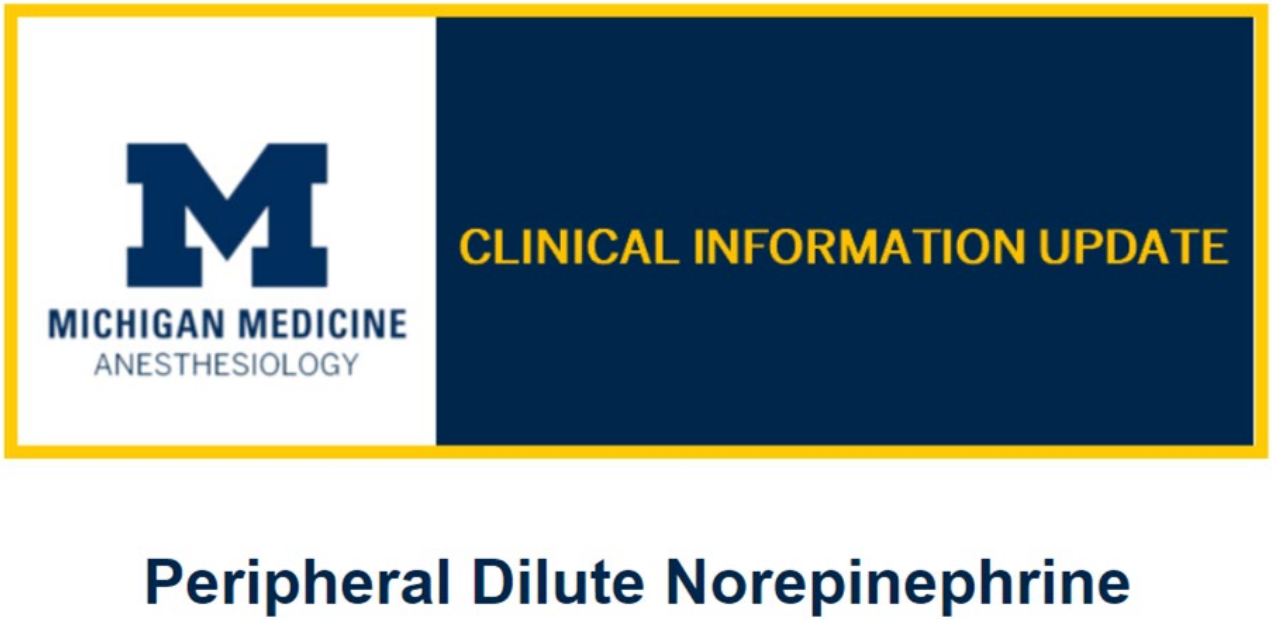
- Phenylephrine (peripheral or central)
- Ephedrine (peripheral or central)
- Vasopressin (ideally central)
- Concentrated norepinephrine (central only)
- **Dilute norepinephrine (peripheral or central)**
- Epinephrine (ideally central)
- Angiotensin II (central only)

Case example: Dilute Norepinephrine at Michigan Medicine

- Peripheral administration of dilute (4 mcg/ml) norepinephrine for bolus and/or infusion up to 0.08 mcg/kg/min, for use in adult patients in operating rooms and procedural rooms only and access limited to anesthesia providers
- 18g PIV or larger and adequate access to the PIV to assess site

Measures for Implementation

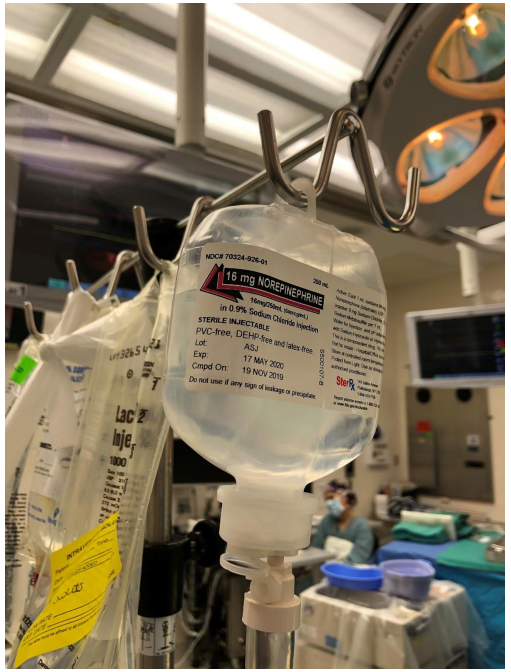
- M&M Conference presentation
- CRNA staff meeting presentation
- Resident lecture presentations for each class
- Multiple small-group presentations for all PACU areas
- Emails and quality & safety announcements



Central Concentrated vs. Dilute Peripheral Dose

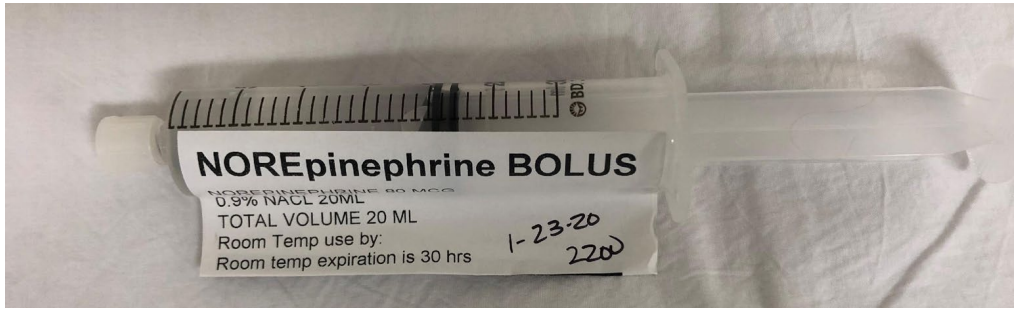
Concentrated for **Central** Access:

- 64mcg/mL
- Only formulation is the infusion bag via central line



Dilute for **Peripheral** Access:

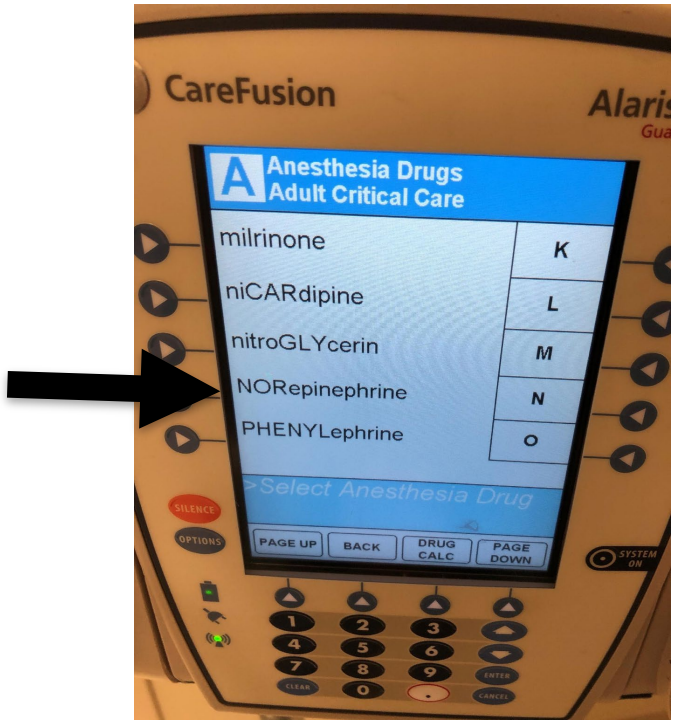
- 4mcg/mL
- May be used as a bolus or as an infusion using syringe pump

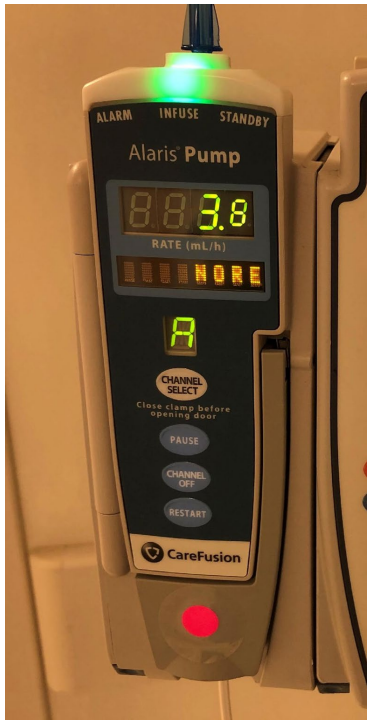


Alaris Pump Changes for Infusions

Concentrated for **Central** Access:

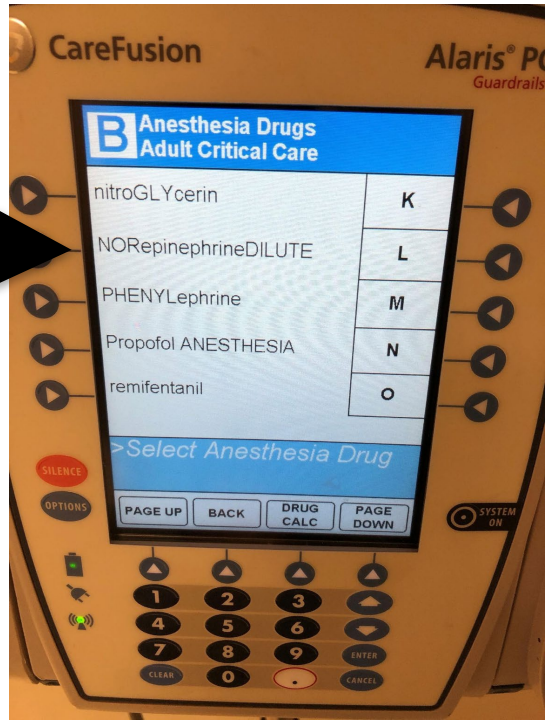
- 64mcg/mL
- **Bag** Alaris Pump Library

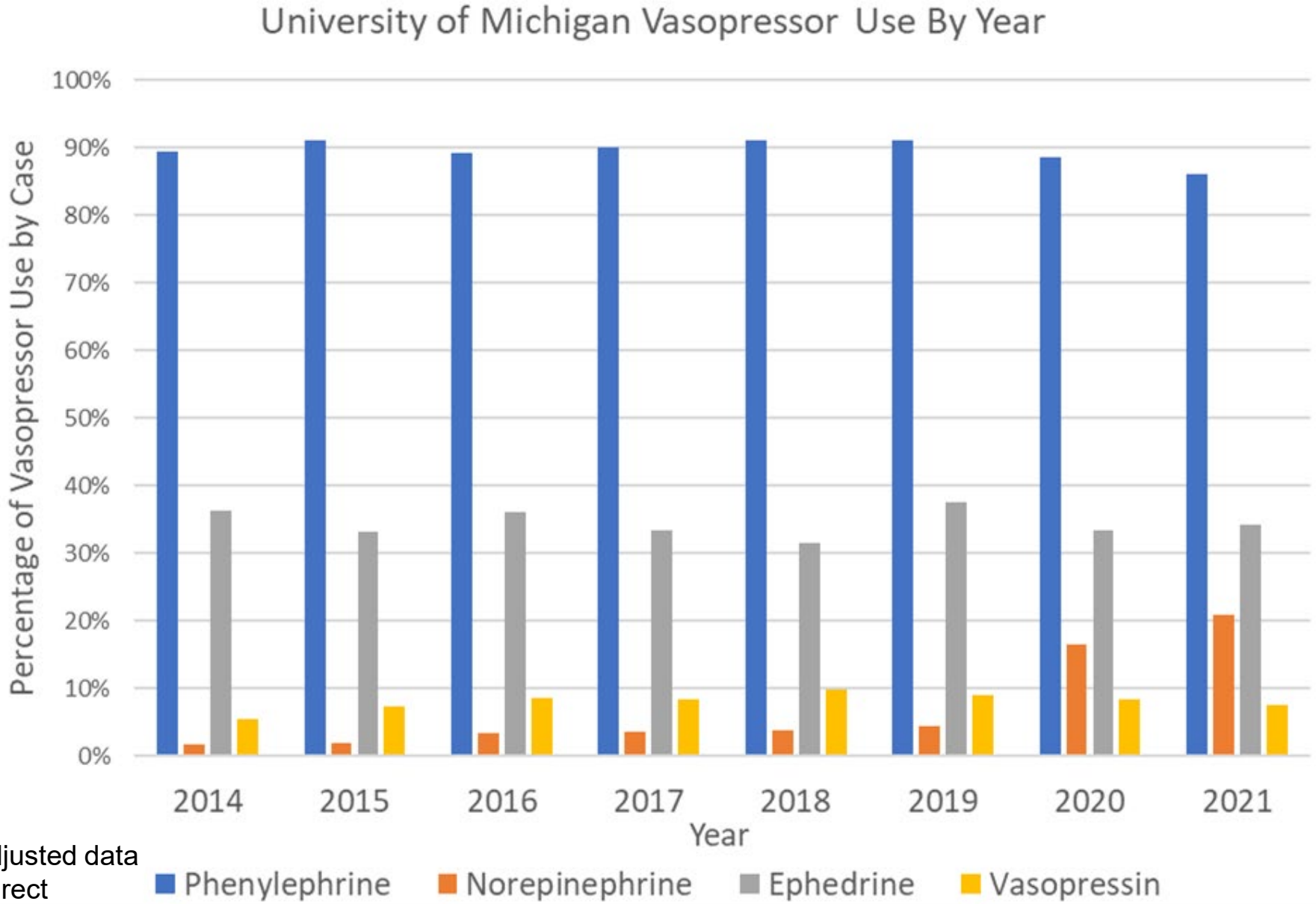




Dilute for **Peripheral** Access:

- 4mcg/mL
- **Syringe** Alaris Pump Library





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Future Studies and Directions

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

NIH National Heart, Lung, and Blood Institute

IARS
International Anesthesia Research Society

Initiative for Multicenter Pragmatic Anesthesiology Clinical Trials (IMPACT)

MPOG
MULTICENTER PERIOPERATIVE OUTCOMES GROUP

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Questions?

Thank you for your time!

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