







Norepinephrine vs Phenylephrine to Prevent AKI

MPOG Retreat - October 10, 2025

Clinical Coordinating Center (UCSF)

Matthieu Legrand, MD PhD (PI)
Michael Bokoch, MD PhD (Study Director)
Niel Panchal (CRC)
Nhu Huynh (CRC)

Data Coordinating Center (Michigan/MPOG)

Sachin Kheterpal, MD, MBA (Co-PI)
Allison Janda, MD (Study Director)
Douglas Colquhoun, MD (Study Director)
Rebecca Pantis (Project Manager)

Disclosures

- No personal consulting, financial, or board membership with any related company
- I am a PI or Co-I on projects that receives or has recently received grant funding from:
 - PCORI
 - NIH
 - NHLBI K23 K23HL166685
 - NHLBI R01HL167790
 - National Library of Medicine 1R01LM01389401
 - NIDDK R01DK133226
 - NIDDK R01DK139484
 - NIH NIGMS T32 Research Fellowship Grant 5T32GM103730-07 (concluded)
 - Haisco-USA Pharmaceuticals, Inc.
 - Bio Intellisense, Inc.









THRIVE (brief) Update















7/1/2023

9/15/2023

3/1/2024

Full Scale Phase Begin Begin Onboarding Full Scale Enrollment Sites First Full Scale Patient Randomized at Wash U or UM End Onboarding Full Scale Enrollment Sites















8/1/2027

11/15/2027

2/1/2028

5/1/2028

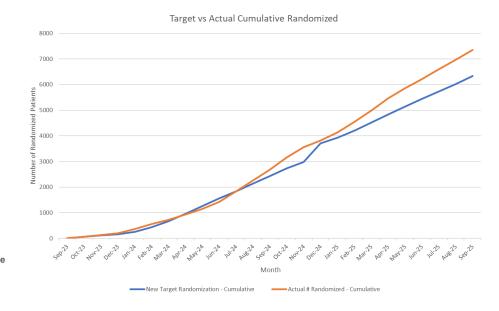
6/30/2028

Complete Randomization

Complete 3 month follow-up

Complete 6 month follow-up, final analytic dataset

All primary analyses funded by PCORI complete Full Scale Phase End









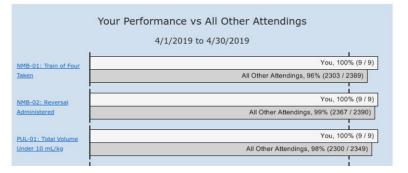


Precision Feedback (brief) Update

- Control: Standard "one-size-fits-most" performance feedback email
- Intervention: "Precisionized" message
- Outcomes: care quality for improvable measures and email engagement (clickthrough and dashboard login rates)
- 48 MPOG sites participated between the pilot study and full trial
 - Thank you!!!
- Data collection is complete and currently analyzing the data

From: mpog-quality@med.umich.edu <mpog-quality@med.umich.edu>
Sent: Wednesday, May 22, 2019 12:04 PM
To:
Subject: MPOG Quality Personalized Performance Report















The choice of vasopressor to prevent postoperative acute kidney injury after major non-cardiac surgery: a multicenter pragmatic cluster cross-over randomized trial

- NIH-funded 10-center pragmatic cluster cross-over randomized trial
- Aim to recruit >18,000 patients over 120 center months
- Compares phenylephrine to norepinephrine
- Primary outcome: Acute Kidney Injury









Thank you for engagement across MPOG!

- Invited sites include:
 - Duke University
 - Henry Ford Health System
 - University of California San Francisco
 - University of Maryland
 - University of Michigan

- University of Texas Southwestern
- University of Toronto
- University of Virginia
- University of Washington
- Wake Forest









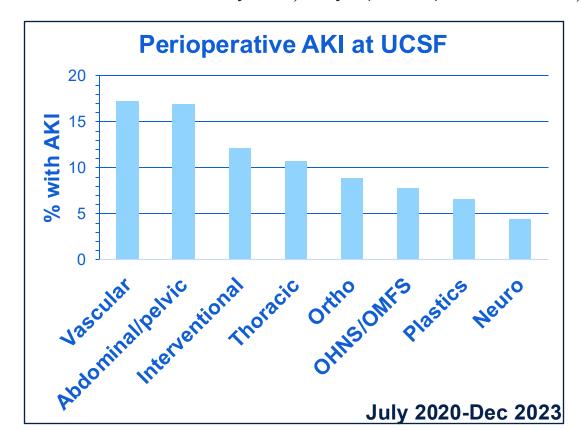
Background and VEGA-1







Acute Kidney Injury (AKI) after major non-cardiac surgery



- UCSF overall 10.5%
- MPOG centers overall 9.0% (range 6.8 to 12.3%)

Key knowledge gap:

"Can the choice of vasopressor reduce postoperative AKI?"



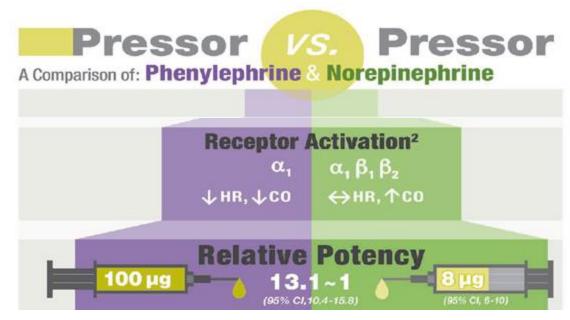




Two 1st-line vasopressors with different pharmacodynamics

 NE improves renal blood flow & outcomes in septic shock

- One RCT has directly compared these in noncardiac, non-obstetric surgery
- → VEGA-1 Trial
- → UCSF + UCLA 2021



Wanderer JP and Rathmell JP (2017) Anesthesiology









"Vasopressor of the Month" Trial



norepinephrine 8 mcg/mL

DATE: Feb. 4, 20 INIT: TIME: 1 2 3 4 5 6 7 8 9 10 11 12 AM PM'

VS.

phenylephrine 100 mcg/mL

DATE: Nov. 4, 20 INIT:

TIME: 123456789101112 AM PM



Legrand M et al., British Journal of Anaesthesia, 130 (5): 519-527 (2023)



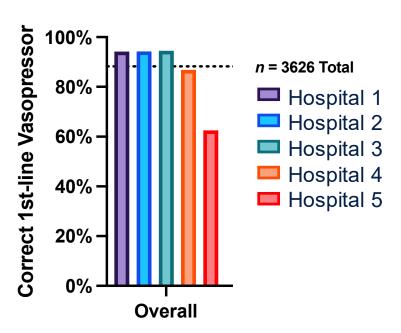




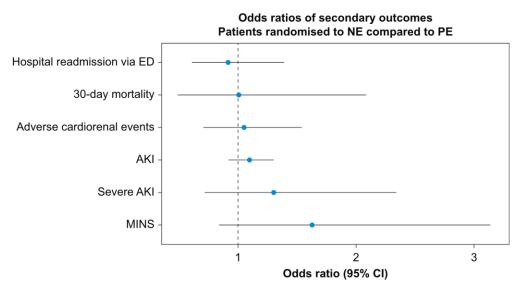


VEGA-1 Results

Primary Outcome (Compliance)



Secondary Outcomes





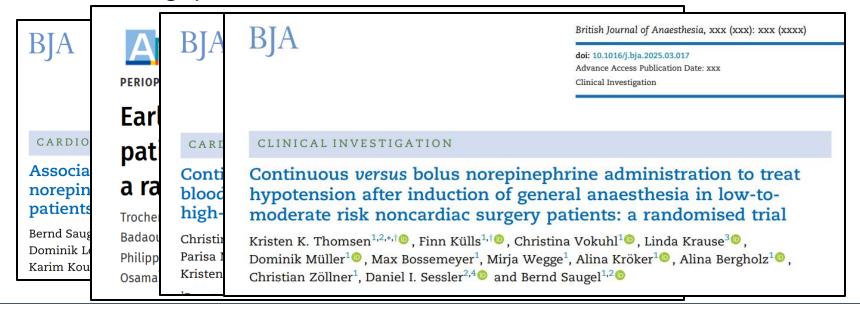






The question remains...

 Recent trials and observational studies validate interest and a continued gap that VEGA-2 will address











The VEGA-2 trial

https://clinicaltrials.gov/study/NCT06802224

R01DK139484



VEGA-2 trial overview

- Aim to recruit 18,000-36,000 patients over 120 center months
- 10 centers (MPOG sites) across North America, 14 months each (2 months run-in)
- 90% power to detect a 1.5% absolute difference in AKI

Intervention:

- Use 1 of 2 first-line vasopressors for <u>INFUSIONS</u> and <u>BOLUSES</u> in major non-cardiac surgery
 - Norepinephrine (4-16 mcg/mL)*
 - Phenylephrine (100-200 mcg/mL)*

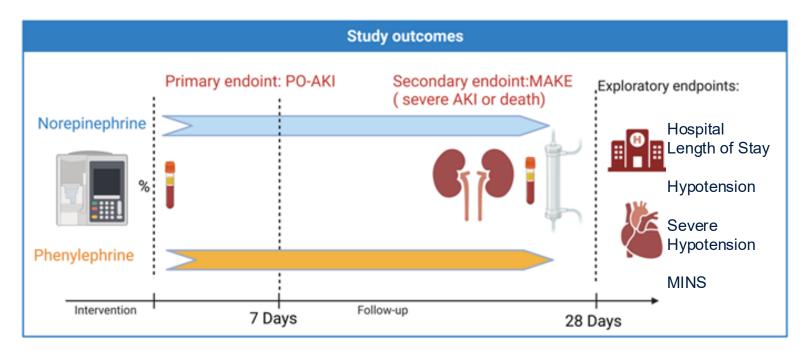








VEGA-2 Trial Outcomes



AKI as defined by KDIGO (creatinine-based) criteria



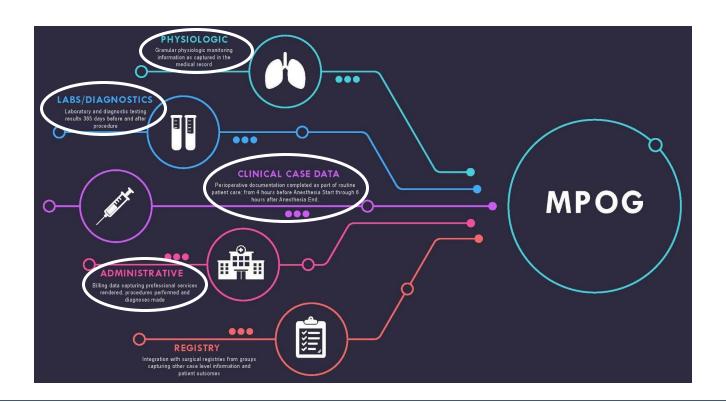






VEGA-2 Data Flow & Processing WPD 5













VEGA-2: broad eligibility

Inclusion criteria

- Age ≥ 18
- Surgery > 2 h under General Anesthesia

Central IRB>
Approved waiver of individual consent!

Exclusion criteria

- Cardiac, ECMO, obstetric, transplant, or procedures on the kidney
- Outpatient procedures
- ASA status 5 or 6, end-stage renal disease, or on vasopressors prior to surgery
- Local protocol at your Center that recommends a specific vasopressor
- Eligibility automatically determined from EMR afterwards
 - You don't have to worry about eligibility of any individual patient









VEGA-2: Cluster Randomized Cross-over Design

	Month		Month						
	1	2	3	4	5	6	7		14
UCSF	NE	PE	NE	PE	NE	PE	NE	1	PE
Univ. of Michigan	PE	NE	PE	NE	PE	NE	PE		NE





VEGA-2: Cluster Randomized Cross-over Design

	Month	***	Month						
	1	2	3	4	5	6	7		14+
UCSF	NE	PE	NE	PE	NE	PE	NE		PE
Univ. of	DE	NE	DE	NE	DE	NE	25		NE
Michigan	PE	NE	PE	NE	PE	NE	PE		NE
Center #3		A	NE	PE	NE	PE	NE		PE
Center #10					NE	PE	NE		PE



VEGA-2: Cluster Randomized Cross-over Design

	Month 1	Month 2	Month 3	Month 4	Month 5	Month 6	Month 7	 Month 14+
UCSF	NE	PE	NE	PE	NE	PE	NE	PE
Univ. of Michigan	PE	NE	PE	NE	PE	NE	PE	NE
Center #3			NE	PE	NE	PE	NE	PE
	R	un-in	Perio	d				
Center #10	(1 ^s	t two	montl	ns)	NE	PE	NE	PE



VEGA-2 Current Status







VEGA-2 trial status update

- Funding awarded September 2024
- As of October 2025:
 - 4/10 sites active
 - UCSF, University of Michigan, University of Virginia, University of Maryland
 - Adherence is excellent due to the hard work of site PIs and MPOG community
 - 2 sites "going live" on 11/1/2025
 - University of Texas Southwestern, Wake Forest
 - Actively onboarding the 4 remaining sites
 - 12/120 center months underway (10% by the end of October!)
 - > 6,000* patients included (*this includes pilot months)









VEGA-2 trial status update

Monthly emails at time of vasopressor change

Emails on the 1st Monday of each month for vacations the prior wee

Morning page the day of the vasopressor change

Badge cards

Posters (ORs, lounges, tech rooms, pharmacy and pharmacy anter

MiChart reminders in the side panel

Reminder cards in OR anesthesia cart clear bins

Reminder cards on the Pyxis

Bin of the "vasopressor-of-the-month" on the pharmacy window led

Anesthesia monitor displays

Reminder treats!











VEGA-2 trial status update

- Adherence estimates are outstanding
 - >84% "vasopressor of the month" adherence across active sites*
 - *includes pilot months and washout days at the beginning of each month
- Intended to include 10 centers (MPOG sites) across North America, 14 months each (2 months run-in) with staggered "go-live"
 - Last pair of sites "go-live" by May 2026
 - Intervention period will continue through June 2027











Thank You and Questions?







