

Evidence-based use of peripheral vasopressors

Elizabeth Munroe, MD, MSc
University of Michigan

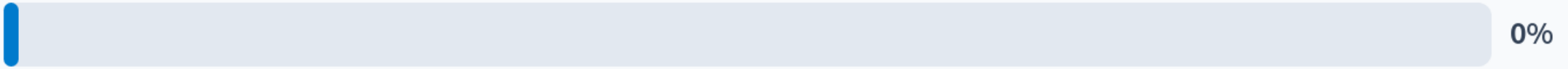
Disclosures None

Agenda

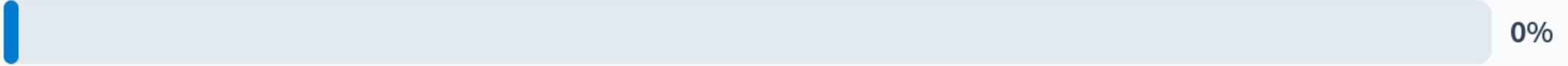
- Review guidelines about vasopressor administration route
- Highlight keys to safe peripheral vasopressor use
- Take a look at current practices

How do you start vasopressors?

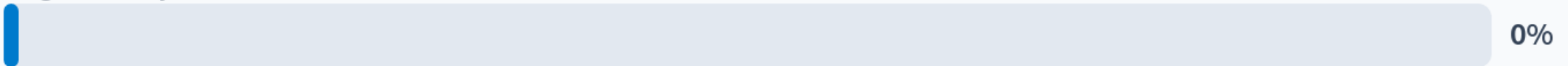
A Place a central line then start vasopressors centrally



B Start vasopressors peripherally but place central line ASAP



C Start vasopressors peripherally and only place a central line if a patient's vasopressor requirements are high or they have another indication for central access



How would you start vasopressors in this patient?

Traditional ← A. Place a central line then start vasopressors centrally

2021 SSC ← B. Start vasopressors peripherally but place a central line asap

New alternative? ← C. Start vasopressors peripherally and only place a central line if patient's vasopressor requirements are high or there is another indication for access



44. For adults with septic shock, we **suggest** starting vasopressors peripherally to restore MAP rather than delaying initiation until a central venous access is secured.

Weak recommendation, very low quality of evidence.

Remark:

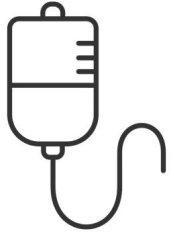
When using vasopressors peripherally, they should be administered only for a short period of time and in a vein in or proximal to the antecubital fossa.

How we give vasopressors is changing

Central —————→ **Peripheral**

1. Concerns about fluid overload → Early vasopressor initiation
2. Awareness of CLABSI and line complications

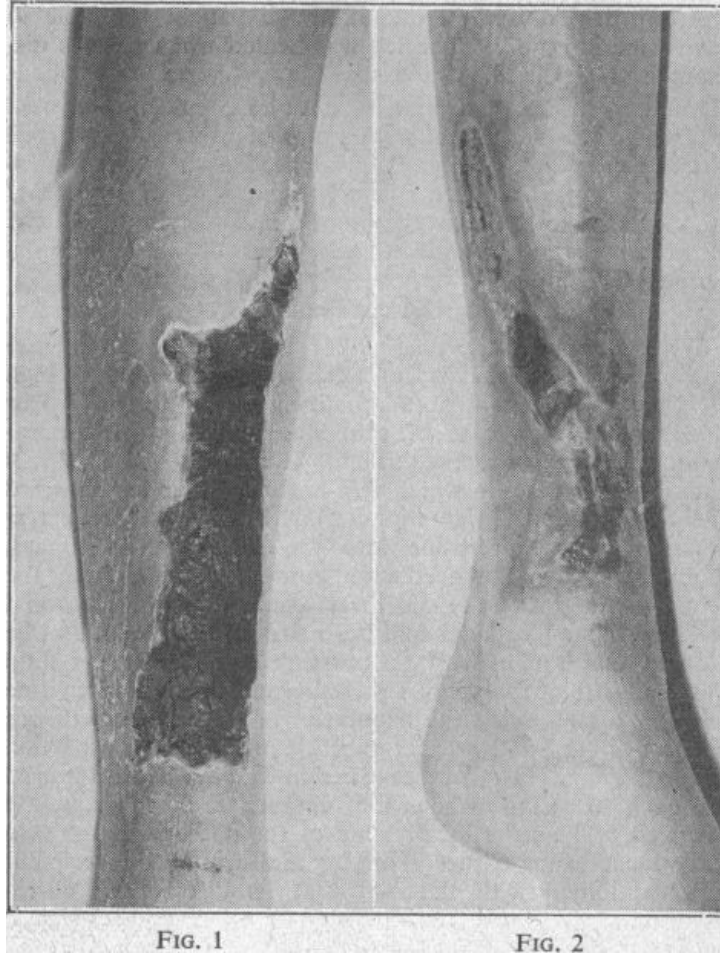
Why central administration?



Norepinephrine label:

Infuse LEVOPHED into a large vein. Avoid infusions into the veins of the leg in the elderly or in patients with occlusive vascular disease of the legs [*see Warnings and Precautions (5.1)*]. Avoid using a catheter-tie-in technique.

Case reports of catastrophic tissue injury



Humphreys et al. *Br Med J*. 1955
Oglesby et al. *Am J Surg*. 1968
Loubani et al. *J Crit Care*. 2015

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How should we give vasopressors?

Central vs **Peripheral**



Disadvantages

- Take time
- Complications (3.1-3.7%)

How should we give vasopressors?

Central

vs

Peripheral




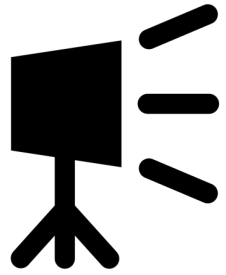
New safety data

Newer safety data

Systematic Review	Patients	Adverse Events	Skin Necrosis or Limb Ischemia
Owen et al, 2021	16,055 ED/ICU and post-op patients	1.8%	0
Tian et al, 2020	1,382 ED/ICU	3.4%	0
Tran et al, 2020	1,835 ED/ICU	7%	0

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Study spotlight

1. Peri-operative study

Retrospective study of 14,385 patients across 2 hospitals in the Netherlands

Patients received peripheral norepinephrine peri-operatively

Durations were short (during surgery)

Results

0.035% (5) extravasations reported with no related complications

2. ICU-based study: Cardenas-Garcia (2015)

Prospective study of 734 ICU patients on vasopressors at a single center

Strict safety protocols

Mean duration: 49 ± 22 hours

Results

Extravasation rate: **2.3%**

No tissue injury

Only 13% required a central line

TABLE 1. Summary of the Requirements for PIV Access Used for Infusion of VM

Vein diameter >4 mm measured with ultrasonography
Position of PIV access documented to be in the vein with ultrasonography before starting infusion of VM
Upper extremity only, contralateral to the blood pressure cuff
Intravenous line size 20 gauge or 18 gauge
No hand, wrist, or antecubital fossa PIV access position
Blood return from the PIV access prior to VM administration
Assessment of PIV access function every 2 hours as per nursing protocol
Immediate alert by nursing staff to the medical team if line extravasation, with prompt initiation of local treatment
72 hours maximum duration of PIV access use

NOTE: Abbreviations: PIV, peripheral intravenous; VM, vasoactive medication.

3. ICU-based study: Yerke (2023)

Prospective study of 635 ICU patients on norepinephrine at a single center

Strict safety protocols



Median duration: 5.8 hours (but up to > 48 hours)

Results

Extravasation rate: **5.5%**

No tissue injury

51.6% avoided a central line

Initial Protocol Requirements (February 2019)

- Two available PIV which are 20 or 22 gauge
- PIV must be placed above the wrist and below the antecubital fossa
- PIV placement must be confirmed via ultrasonography
- Assessment of PIV patency every 2 hours
- Maximum norepinephrine dose of 15 mcg/min
- Maximum infusion time of 48 hours
- Included patients must be able to report pain or discomfort

Peripheral vasopressors appear to be safe

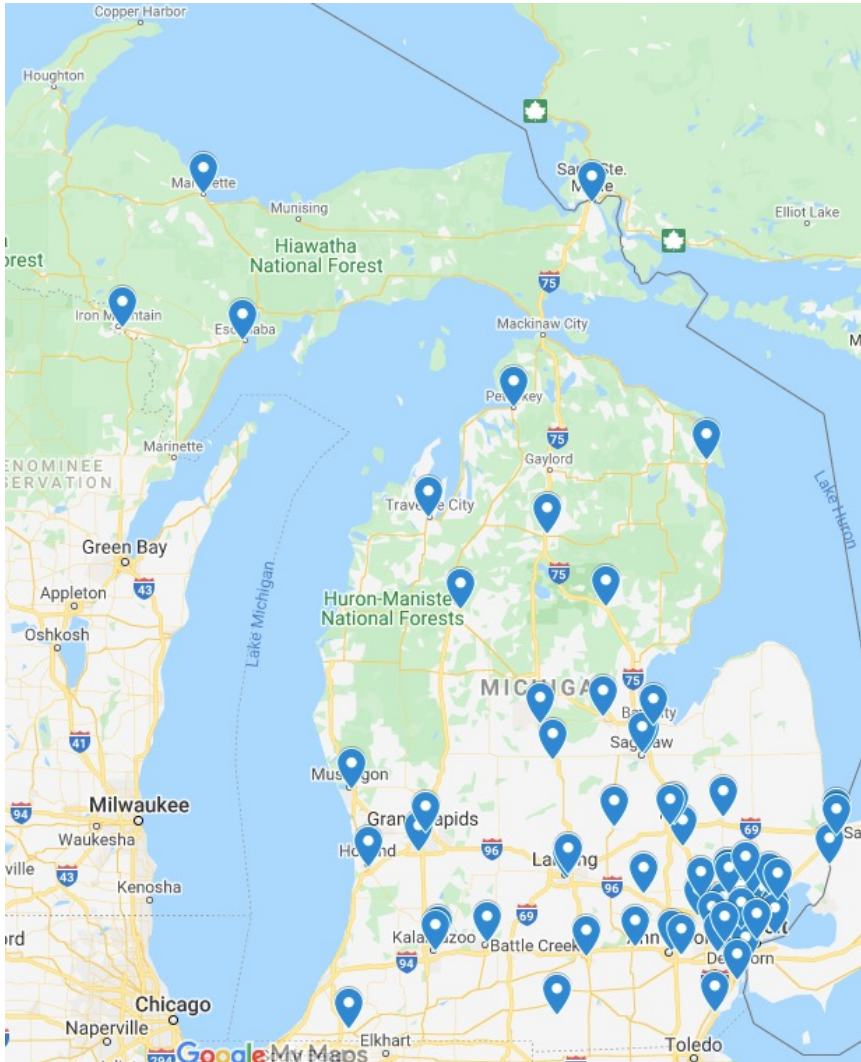
....in single-centered studies with **strict protocols**.

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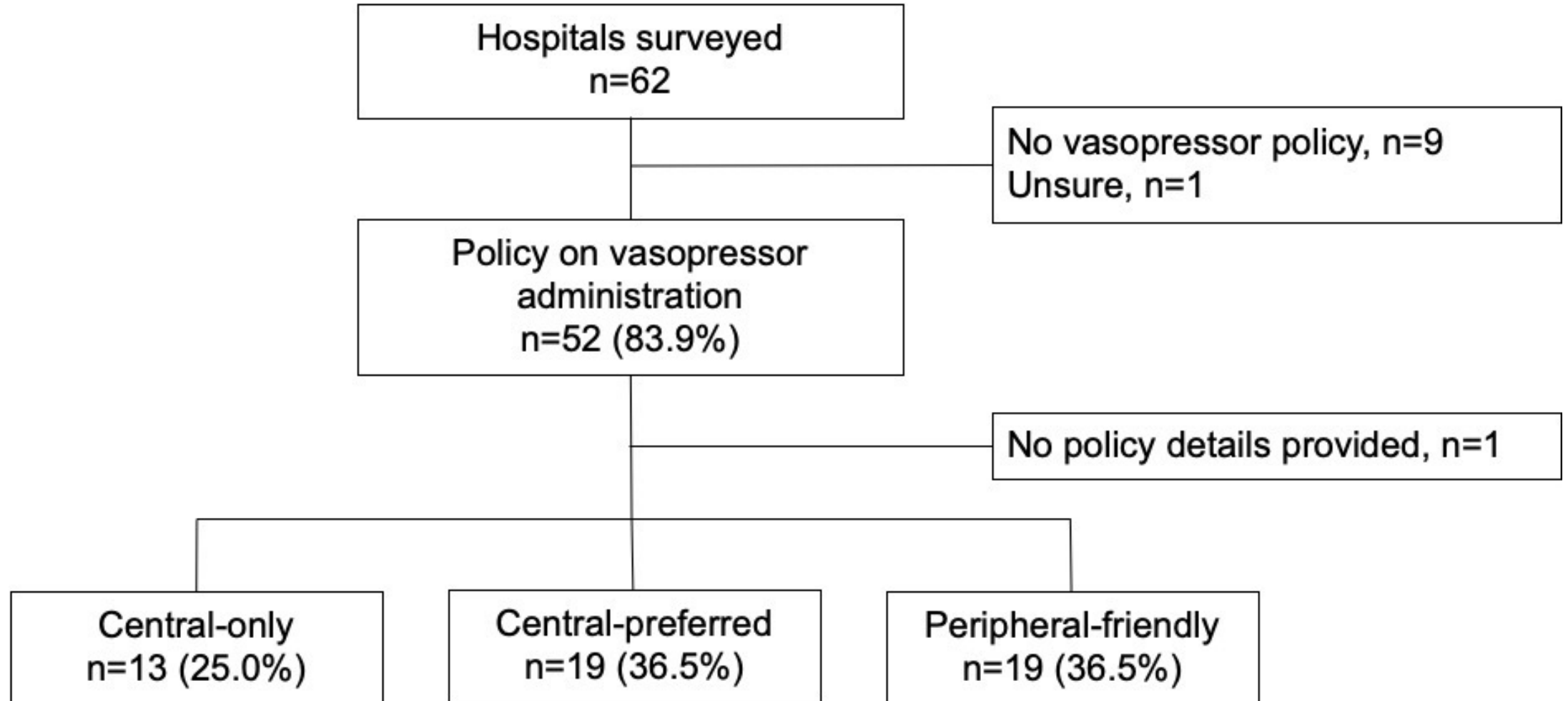
....in single-centered studies with **strict protocols**.

Do hospitals have similar safety protocols?

A survey of hospital vasopressor policies



Hospital vasopressor policies



Policy limits on peripheral vasopressors

```
graph TD; A[Policy limits on peripheral vasopressors] --> B[Vasopressor-based limits]; A --> C[IV-based limits];
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Vasopressor-based limits

- Duration
- Dose
- Agent
 - Type
 - Single agent

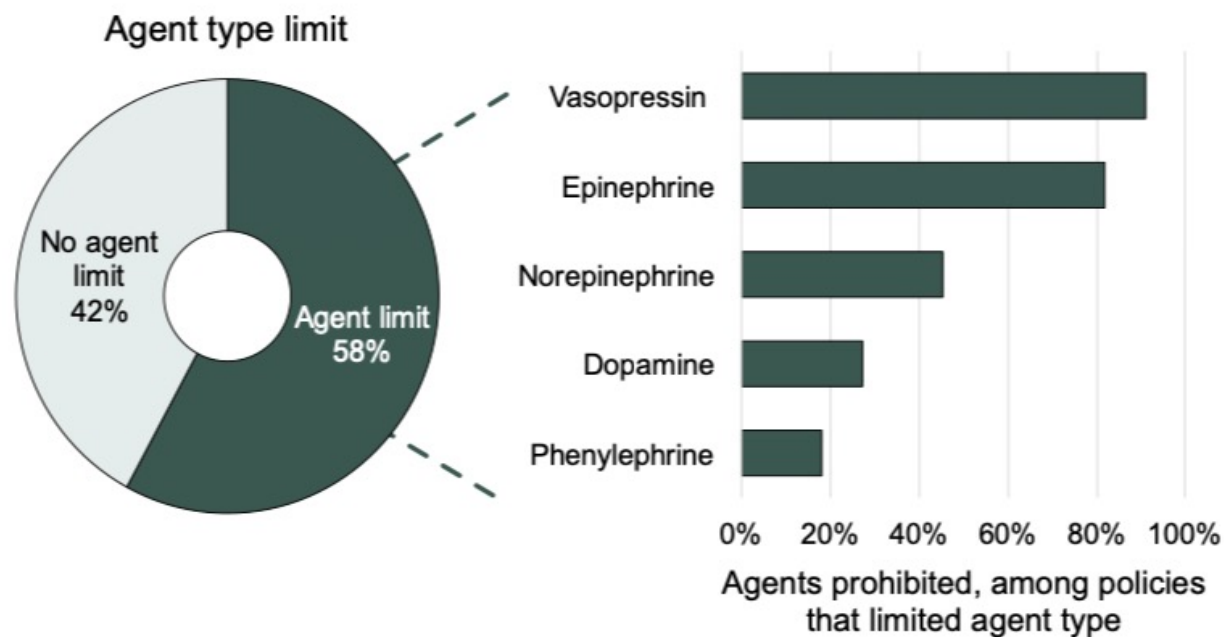
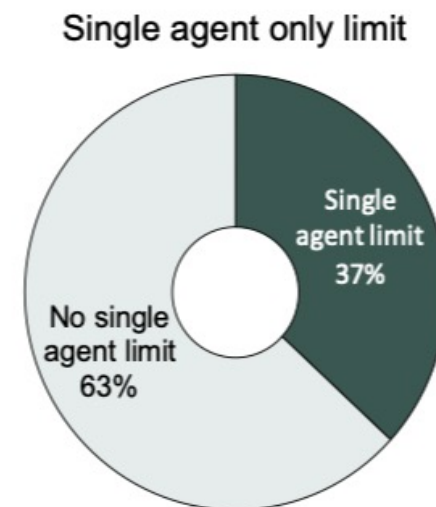
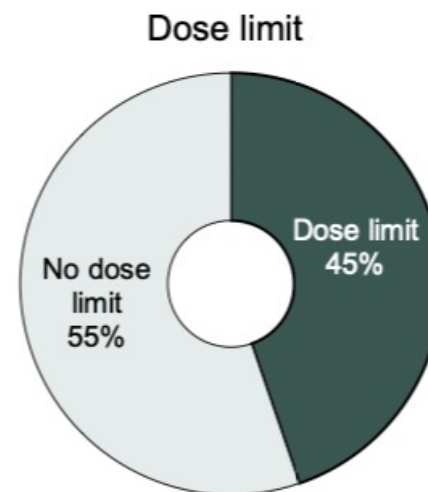
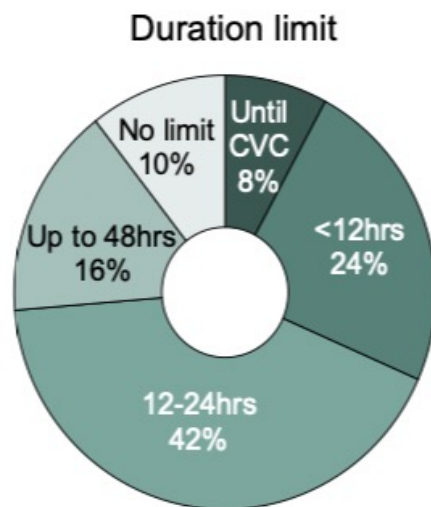
IV-based limits

- IV size
- IV location
- Monitoring
- Ultrasound-guided IV placement

Take-Away: Policies varied widely

Vasopressor Limits

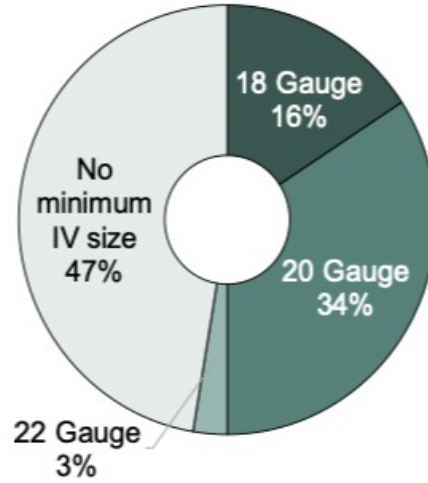
n=38



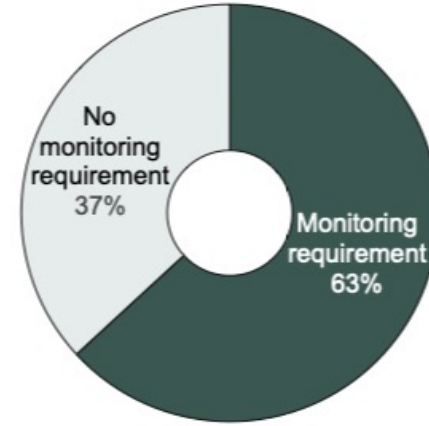
IV Limits

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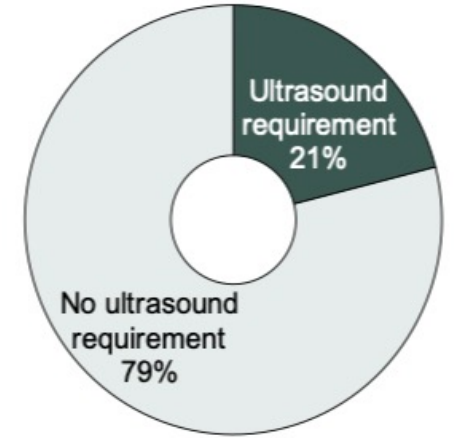
Minimum IV size requirement



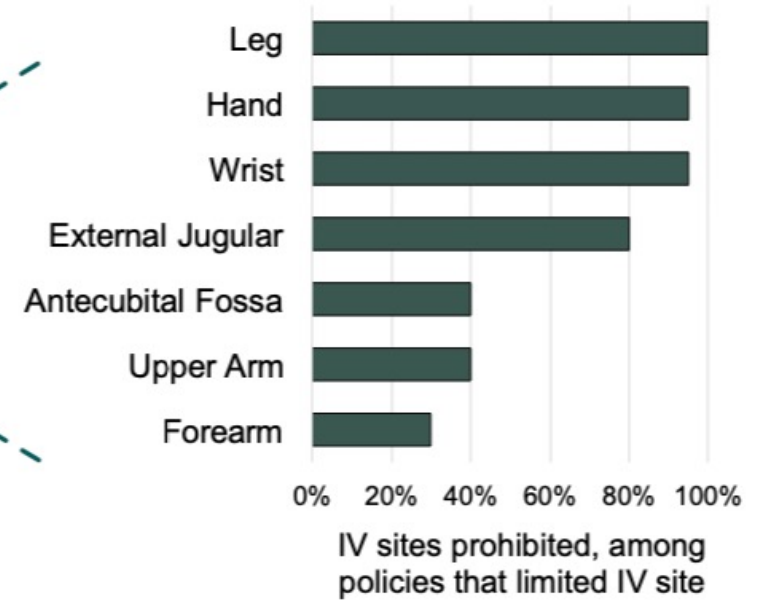
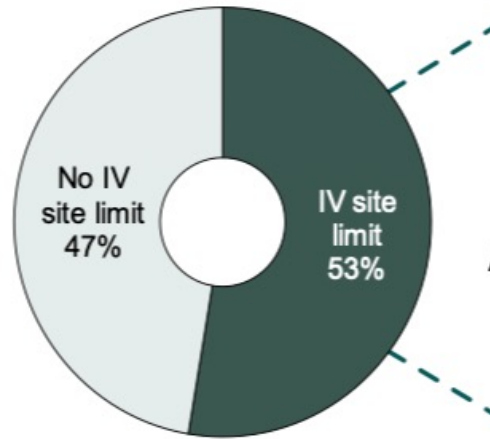
IV monitoring requirement



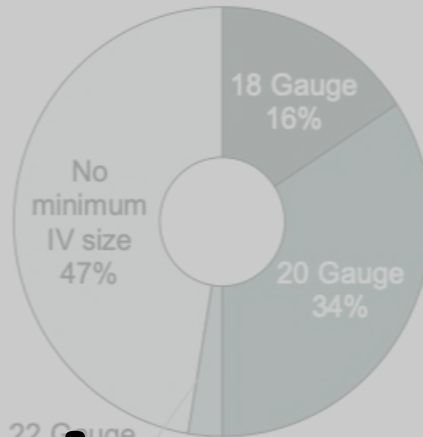
Ultrasound IV requirement



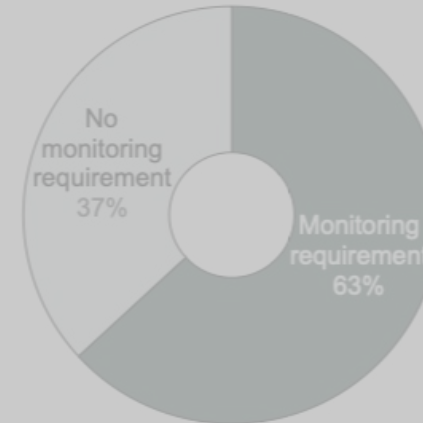
IV site limit



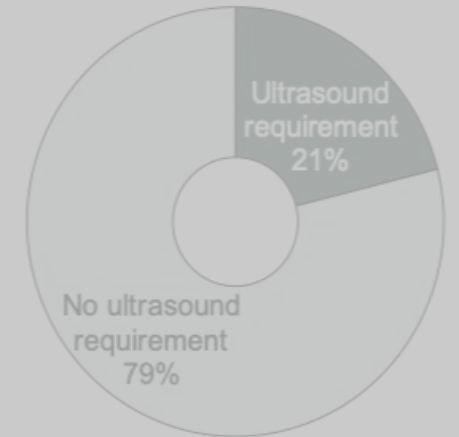
Minimum IV size requirement



IV monitoring requirement



Ultrasound IV requirement



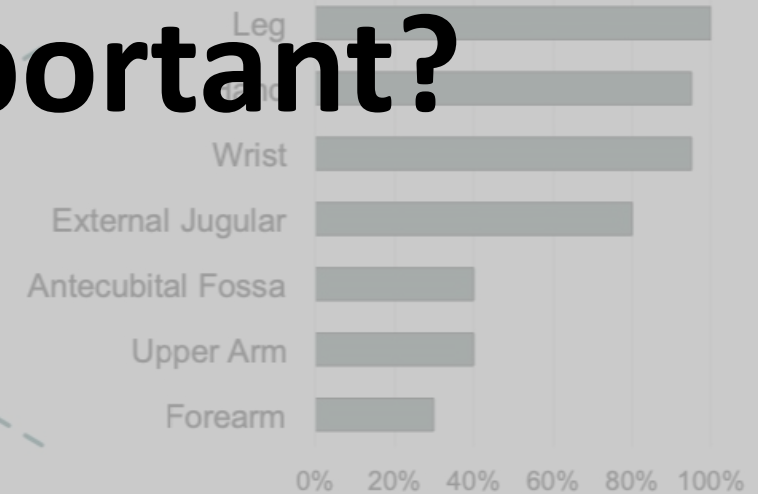
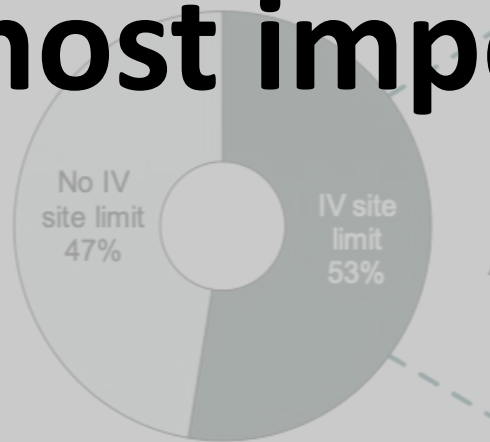
IV Limits

n=38

Policies vary widely.

What is most important?

IV site limit



IV sites prohibited, among policies that limited IV site

What is most important?



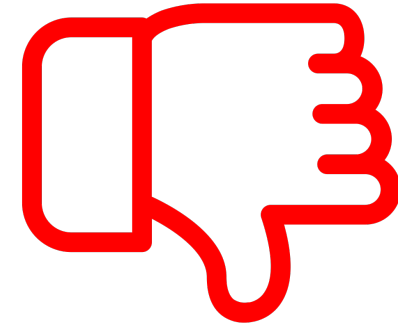
Definitely needed

Monitoring
Extravasation
management plans



May be needed

Dose caps
Duration limits
PIV requirements



Not needed/harmful

Agent restrictions

What is most important?



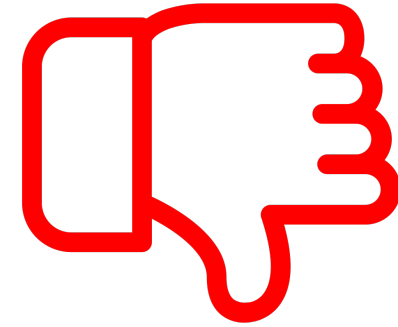
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Monitoring

Rationale: Extravasation happens. Catching it early prevents tissue injury.

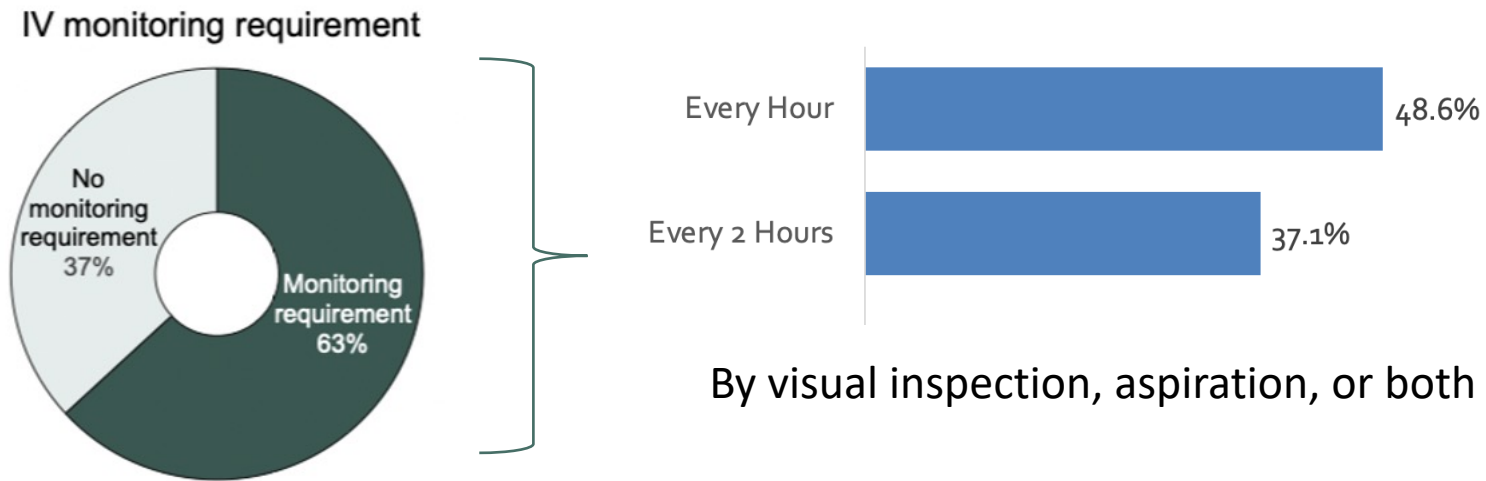
- Studies have required monitoring every 2 hours “for patency”



Monitoring

Rationale: Extravasation happens. Catching it early prevents tissue injury.

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Extravasation management plans

Rationale: Extravasation happens. We need to know what to do.

- Studies have included explicit **extravasation management plans**
 - Easily accessible phentolamine & nitroglycerin
 - Clear, nursing-driven response protocols
 - Nursing and team education

What is most important?



Definitely needed

Monitoring

Extravasation
management plans

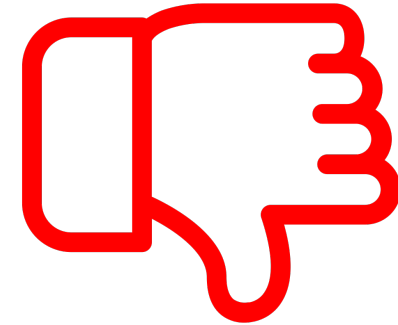


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PIV requirements



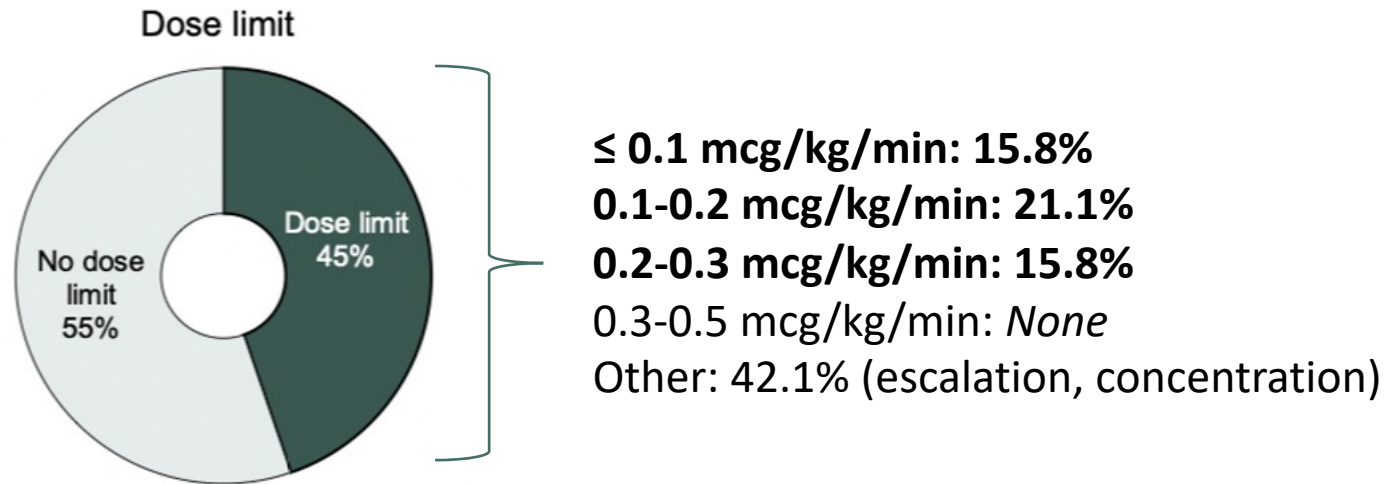
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Agent restrictions



Dose caps

Rationale: Higher doses may be more likely to cause injury





Dose caps

Rationale: Higher doses may be more likely to cause injury

Evidence

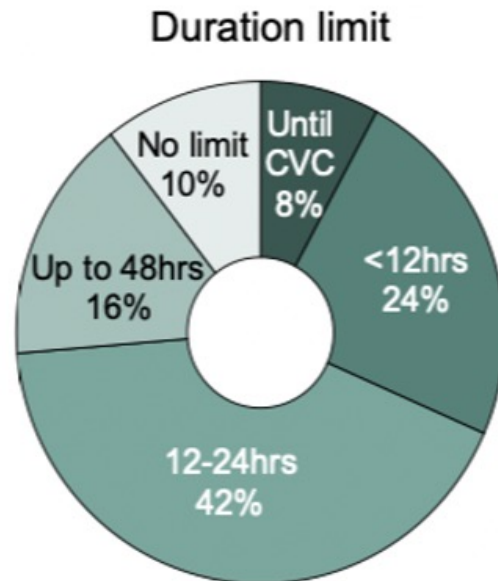
- Most studies cap doses around 0.15-0.3 mcg/kg/min
- Cardenas-Garcia had mean peak 0.7mcg/kg/min with no tissue injury

My practice: Place central line when adding a second vasopressor



Duration limits

Rationale: Longer duration increases risk of extravasation





Duration limits

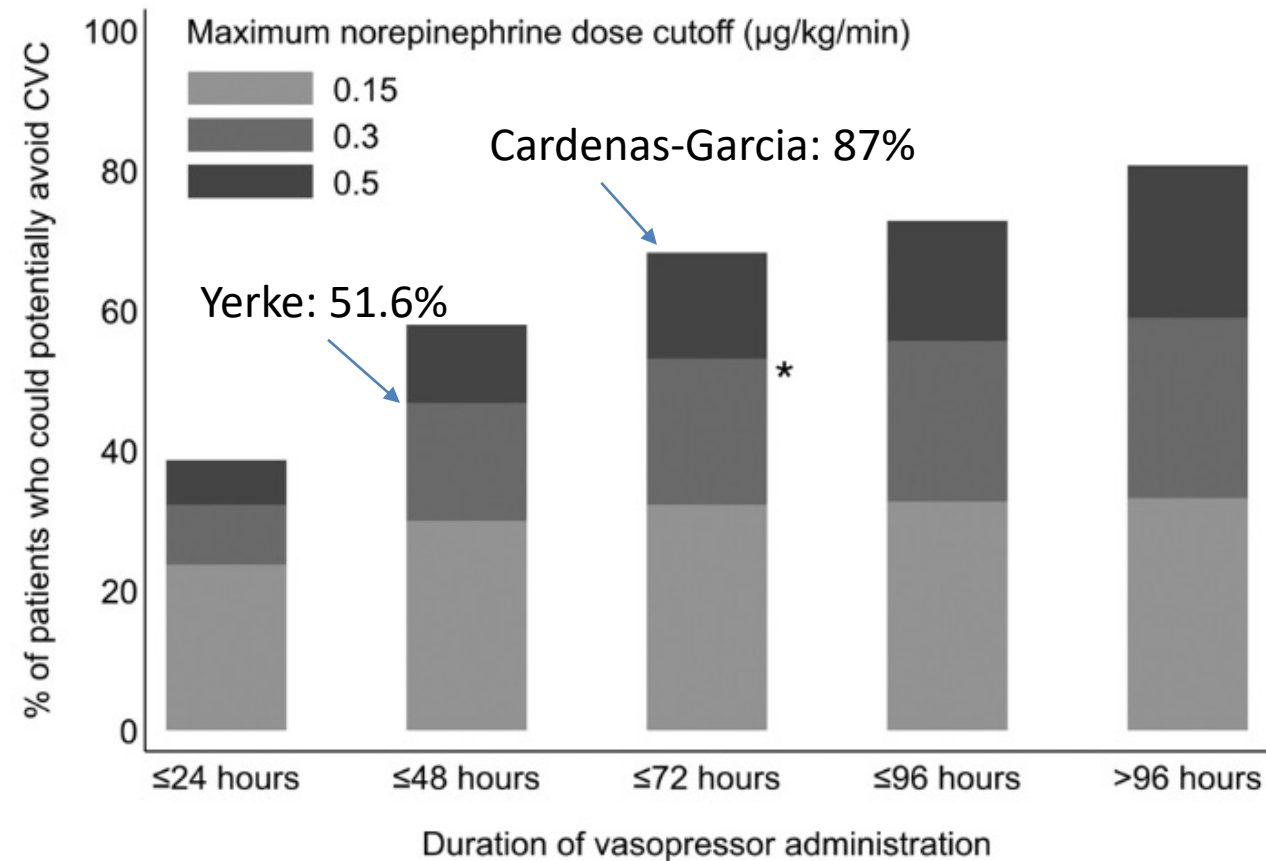
Rationale: Longer duration increases risk of extravasation

Evidence:

- Cardenas-Garcia: mean 49 hours
- Yerke: time of infusion \neq extravasation

My practice: With good monitoring and assessment of IV patency, durations longer than 24 hours are reasonable

Why it matters: Theoretical central line saved with dose and duration limits

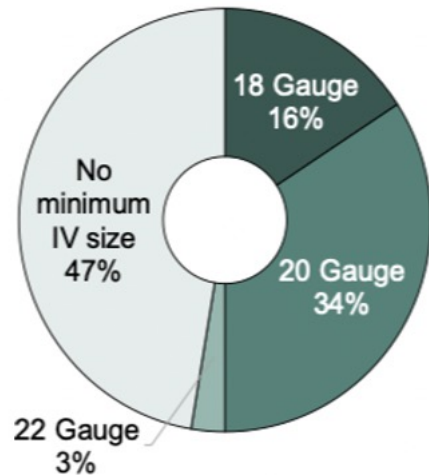




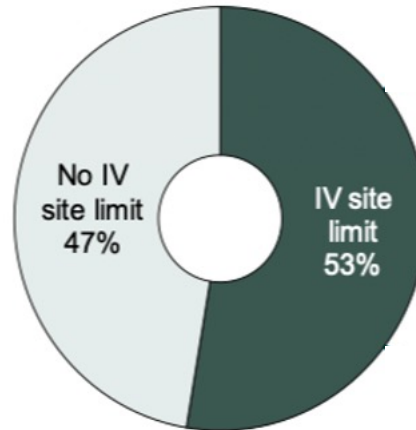
IV requirements

Rationale: Larger, proximal IVs are less likely to extravasate

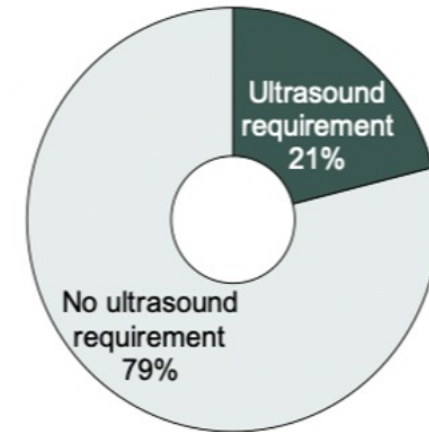
Minimum IV size requirement



IV site limit



Ultrasound IV requirement





IV requirements

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Evidence

- Studied protocols include:
 - PIV 18-20G +
 - Avoid legs, hands
 - Ultrasound confirmation



IV requirements

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→
*But there are
violations & still
safe*

Protocol criteria met at time of norepinephrine initiation	
Catheter size criteria	529 (83.3)
Catheter placement location criteria	422 (66.5)
Catheter ultrasound confirmation criteria	316 (49.8)



IV requirements

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Protocol criteria met at time of norepinephrine initiation	
Catheter size criteria	529 (83.3)
Catheter placement location criteria	422 (66.5)
Catheter ultrasound confirmation criteria	316 (49.8)

My practice: Use large IVs in forearm or upper arm and confirm with ultrasound when possible

What is most important?



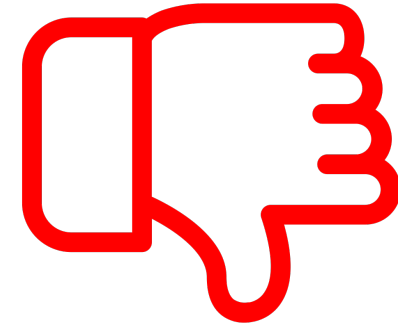
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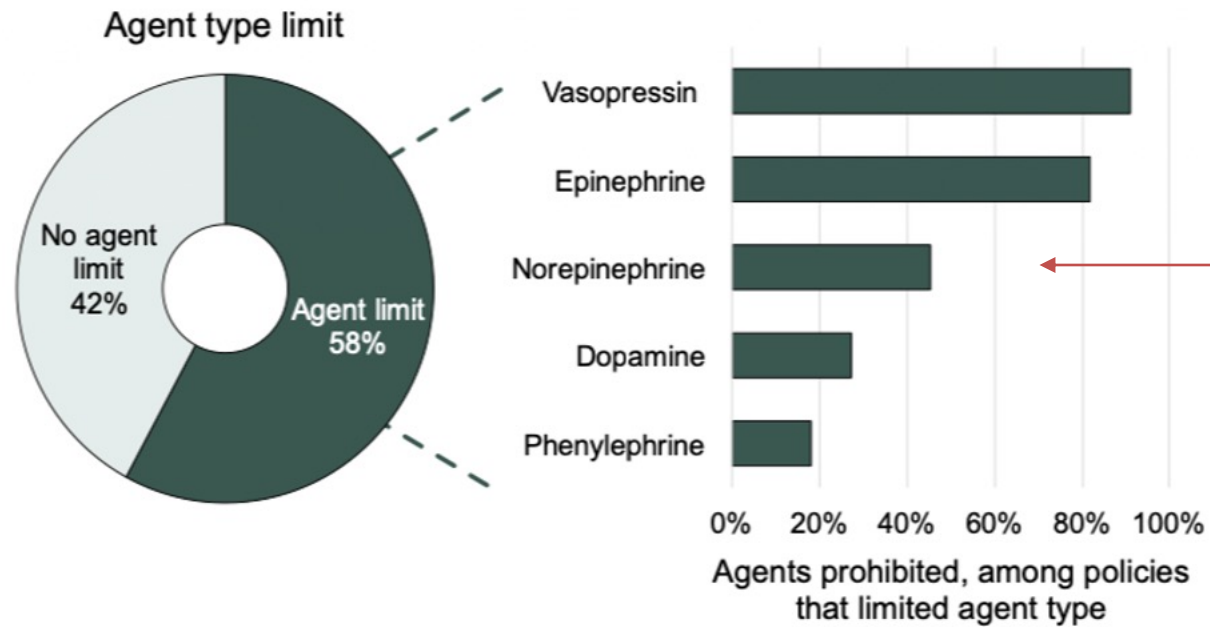


Not needed/harmful

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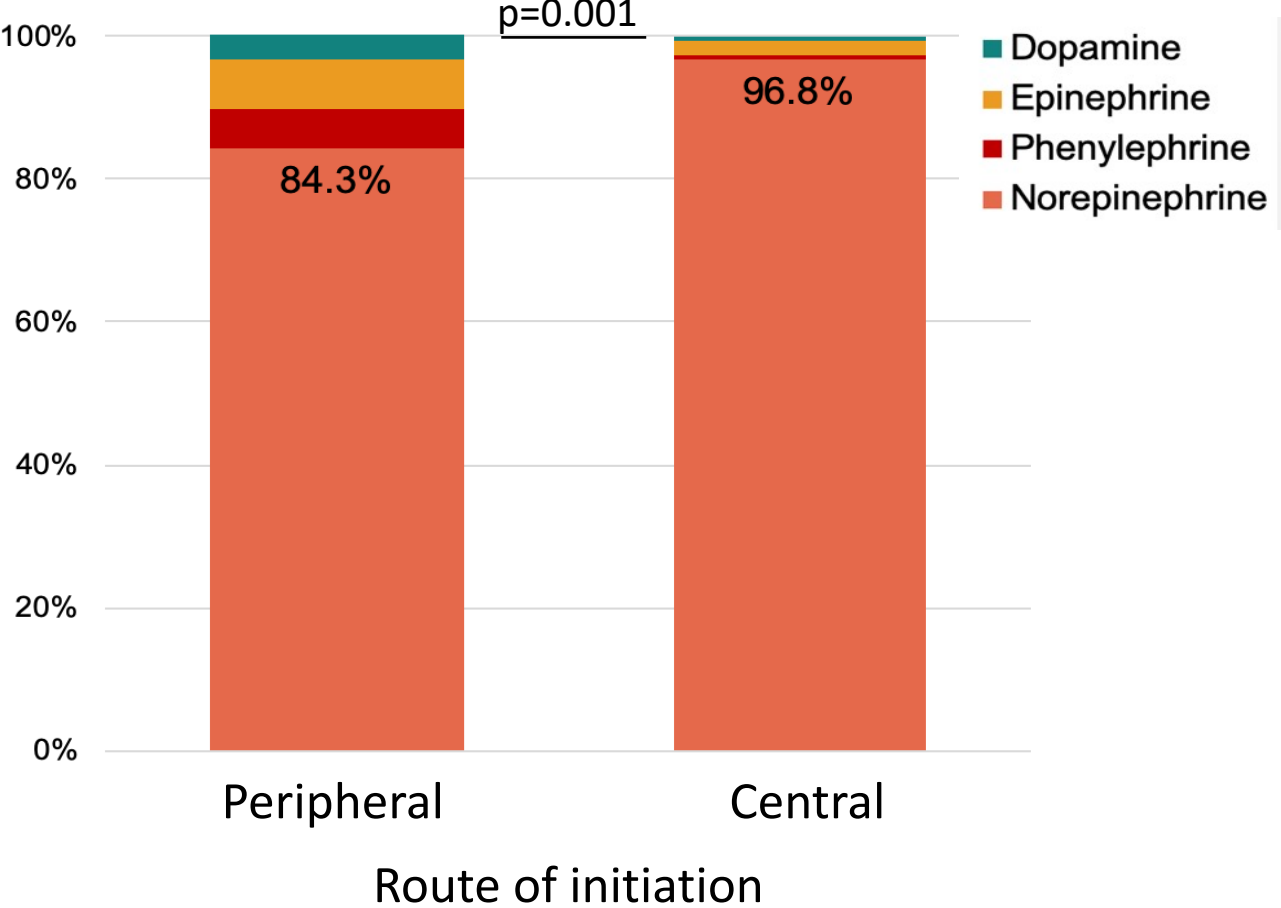


Limits on peripheral norepinephrine



Almost half of hospitals are prohibiting peripheral norepinephrine

Less norepinephrine is used peripherally



Peripheral norepinephrine is the best studied

	Patients	N	
Norepinephrine	ICU/ED	702	+ 635 in Yerke = >1,300 ICU patients
	OR	14,385	
Phenylephrine	ICU/ED	546	
Dopamine	ICU/ED	106	

Using peripheral access is not a reason to avoid norepinephrine!

Using peripheral access is not a reason to avoid norepinephrine!

Surviving Sepsis
Campaign



Use norepinephrine as first-line
vasopressor

Rare strong recommendation!

Vasopressin is a different story

Surviving Sepsis
Campaign

*If MAP is inadequate despite low-to-moderate
dose norepinephrine*



Consider adding vasopressin



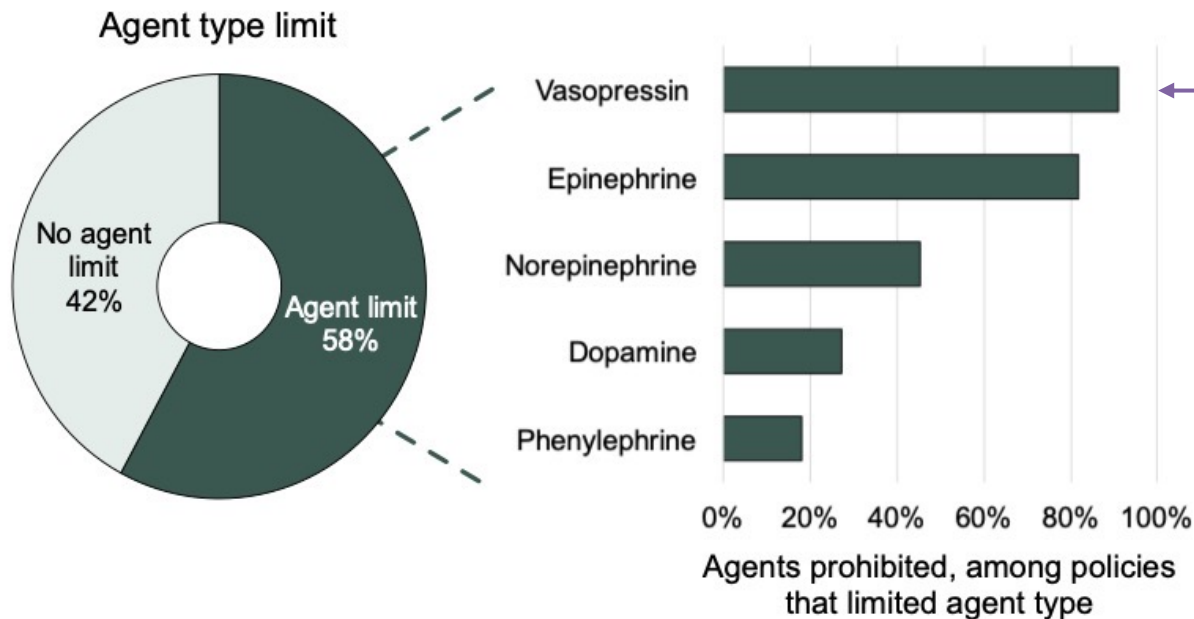
Peripheral vasopressin should be used with caution

- Unlike norepinephrine: no antidote for extravasation, not well studied



Peripheral vasopressin should be used with caution

- Unlike norepinephrine: no antidote for extravasation, not well studied
- Policies often prohibit peripheral use



A majority prohibit peripheral vasopressin

Yet, vasopressin is best in less severe shock

Table 4. Rates and Risks of Death from Any Cause According to the Severity of Shock.*

Stratum	Norepinephrine Group	Vasopressin Group	P Value†
	<i>no./total no. (%)</i>		
More severe septic shock			
28-day mortality	85/200 (42.5)	88/200 (44.0)	0.76
90-day mortality	105/199 (52.8)	103/199 (51.8)	0.84
Less severe septic shock			
28-day mortality	65/182 (35.7)	52/196 (26.5)	0.05
90-day mortality	83/180 (46.1)	69/193 (35.8)	0.04

* Patients with more severe septic shock were defined as those who required at least 15 μg of norepinephrine per minute or the equivalent at the time of randomization. Those with less severe septic shock were defined as those who required 5 to 14 μg of norepinephrine per minute or the equivalent at the time of randomization.

0.07-0.2 mcg/kg/min

Yet, vasopressin is best in less severe shock

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90-day mortality	105/199 (52.8)	103/199 (51.8)	0.84
Less severe septic shock			
28-day mortality	These are the patients who may avoid central lines with peripheral norepinephrine!		
90-day mortality			

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0.07-0.2 mcg/kg/min

What should we do about vasopressin?

We need more data on peripheral vasopressin safety

In the meantime, place a central line to add vasopressin



There are key elements of peripheral vasopressor safety protocols.

... but actual hospital policies vary widely.

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... but actual hospital policies vary widely.

What are providers doing in practice?

CLOVERS gives us a window into practice

- Multi-center US trial of early vasopressors vs liberal fluids in sepsis-induced hypotension
- Vasopressors could be given using “Large Peripheral IV” or central line, per treating team
 - Presumably with a range of policies

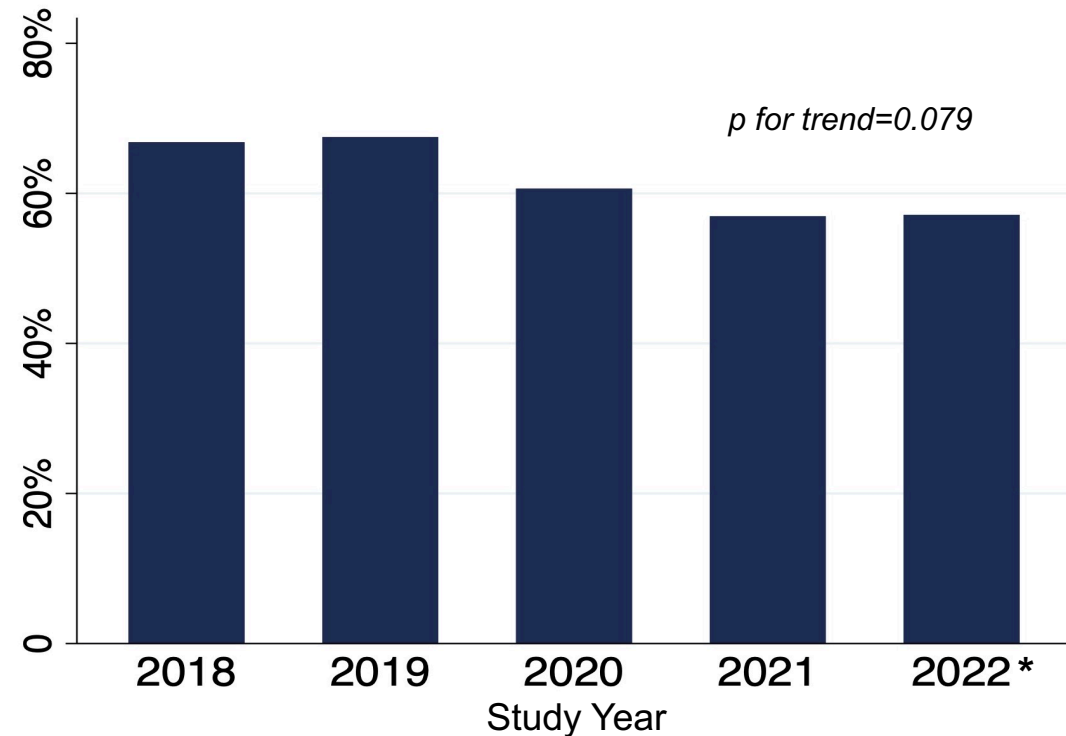


Peripheral vasopressor use in CLOVERS

Figure 1. Peripheral vasopressor use over time

Percent of patients on vasopressors who received a peripheral vasopressor over the study period

Overall,
500/750 (66.6%)
received peripheral
vasopressors



*incomplete year, study ended January 2022

Peripheral vasopressors were very safe

28-day complications in CLOVERS

Peripheral Vasopressors

0.6%

3/490 patients

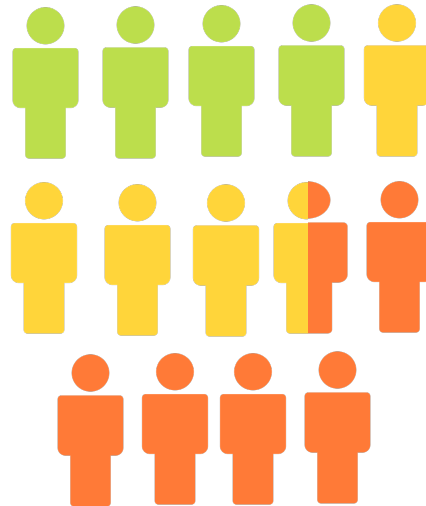


VS




CVC Placement

3.9%

14/363 patients



Key: Complication Grading

-  **Grade 1:** Asymptomatic
-  **Grade 2:** Symptomatic
-  **Grade 3:** Urgent intervention

No Grade 4 (Life-threatening) or Grade 5 (Death)



Peripheral norepinephrine is safe

28-day complications in CLOVERS

Peripheral Vasopressors

0.6%

3/490 patients

96% norepinephrine

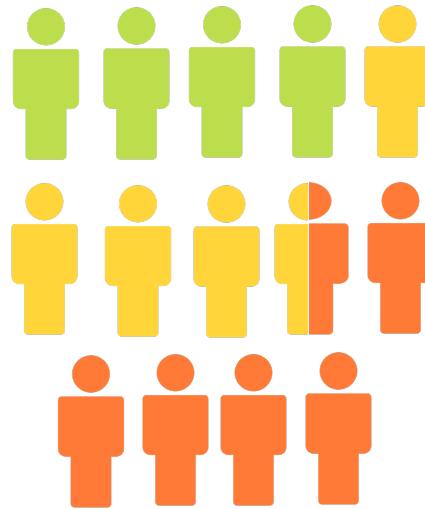


VS

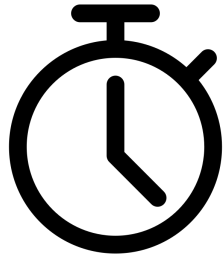
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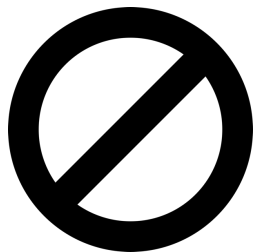
Peripheral initiation had practical advantages*



Faster



Less fluid



Avoid central line

**adjusted for pre-specified patient characteristics, illness severity, study arm*



Munroe work in progress,
please do not share

Peripheral: fast, practical, & safe

Are these findings generalizable?

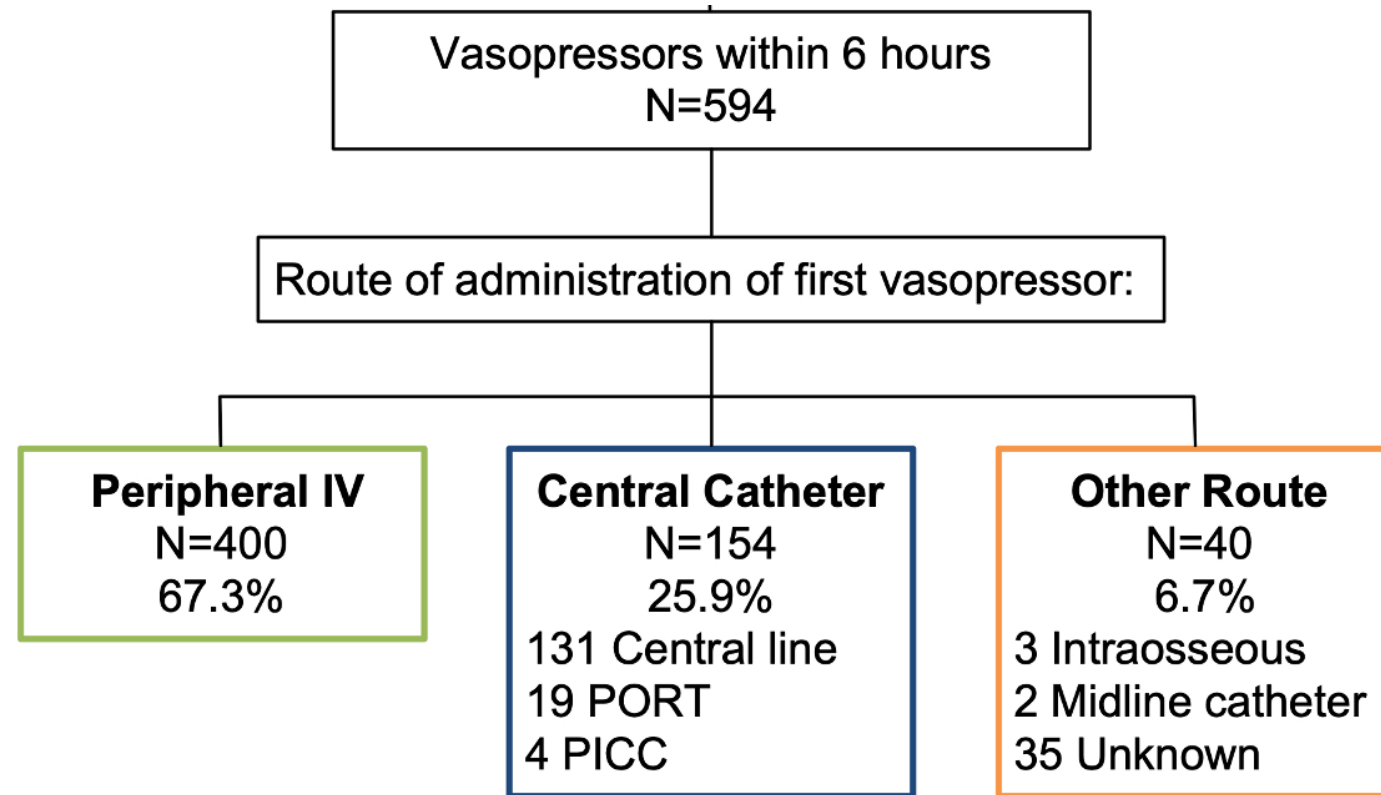
- CLOVERS encouraged peripheral vasopressors

Are these findings generalizable?

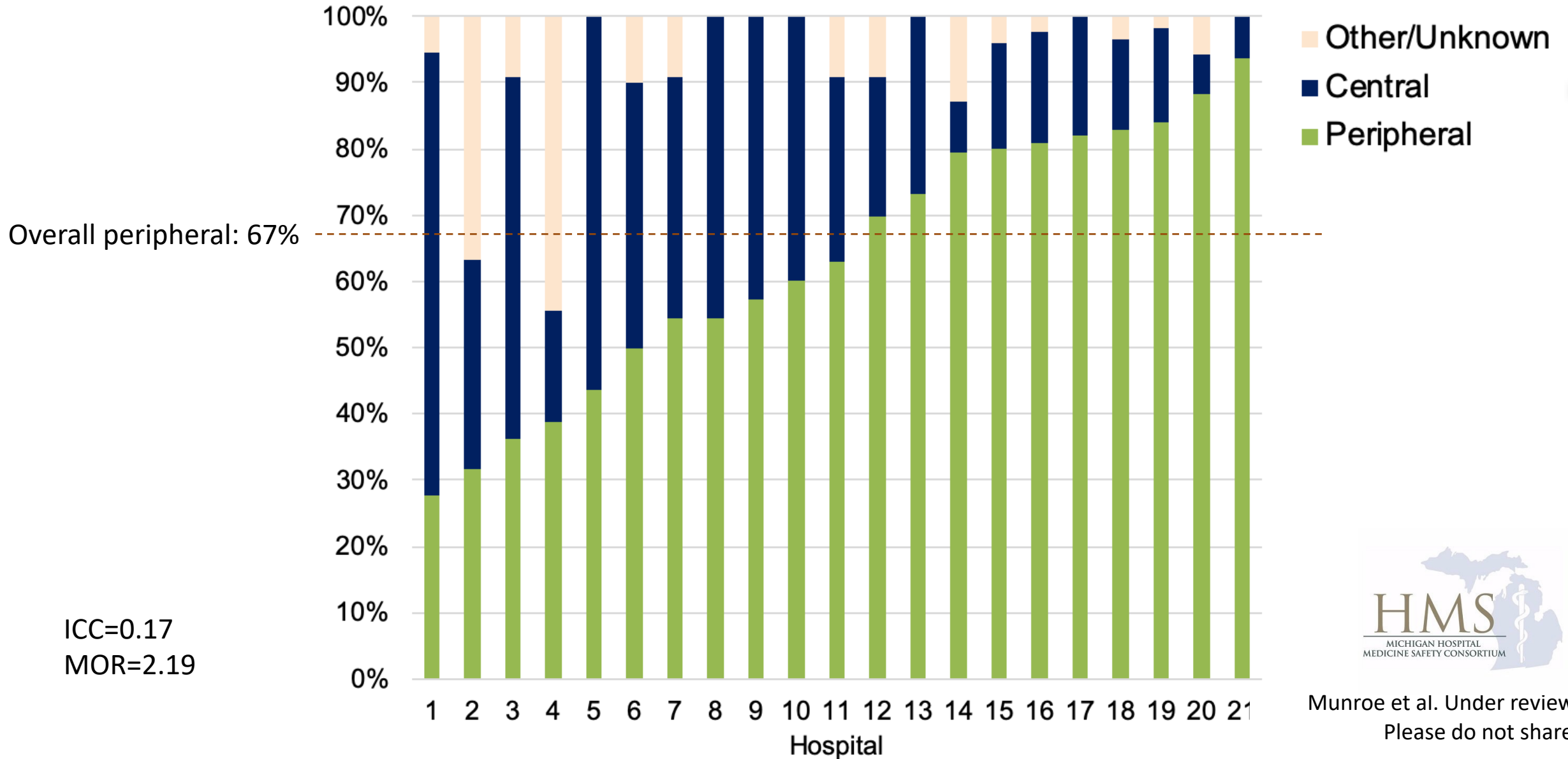
- Retrospective cohort study of Michigan hospitals: similar patterns



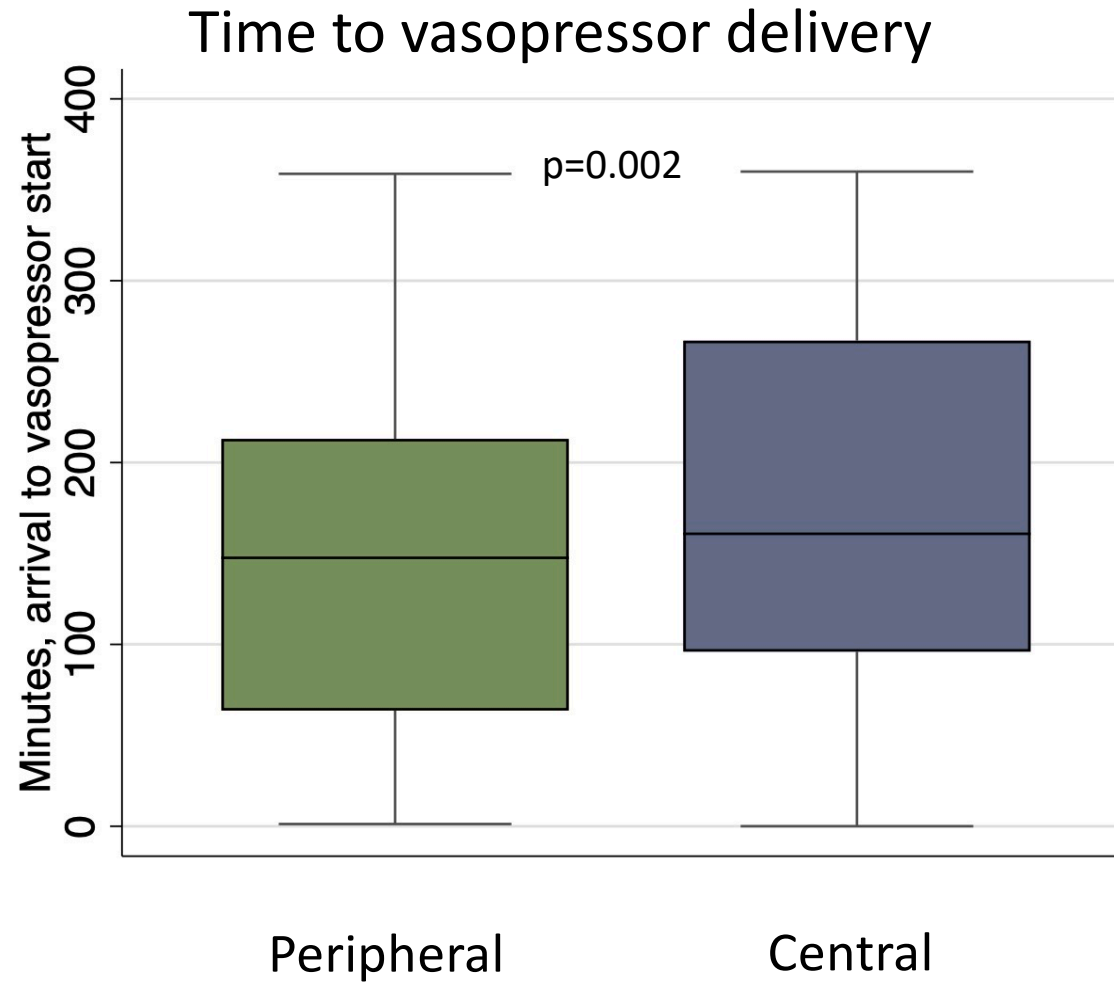
Peripheral initiation was common



Peripheral initiation varied by hospital

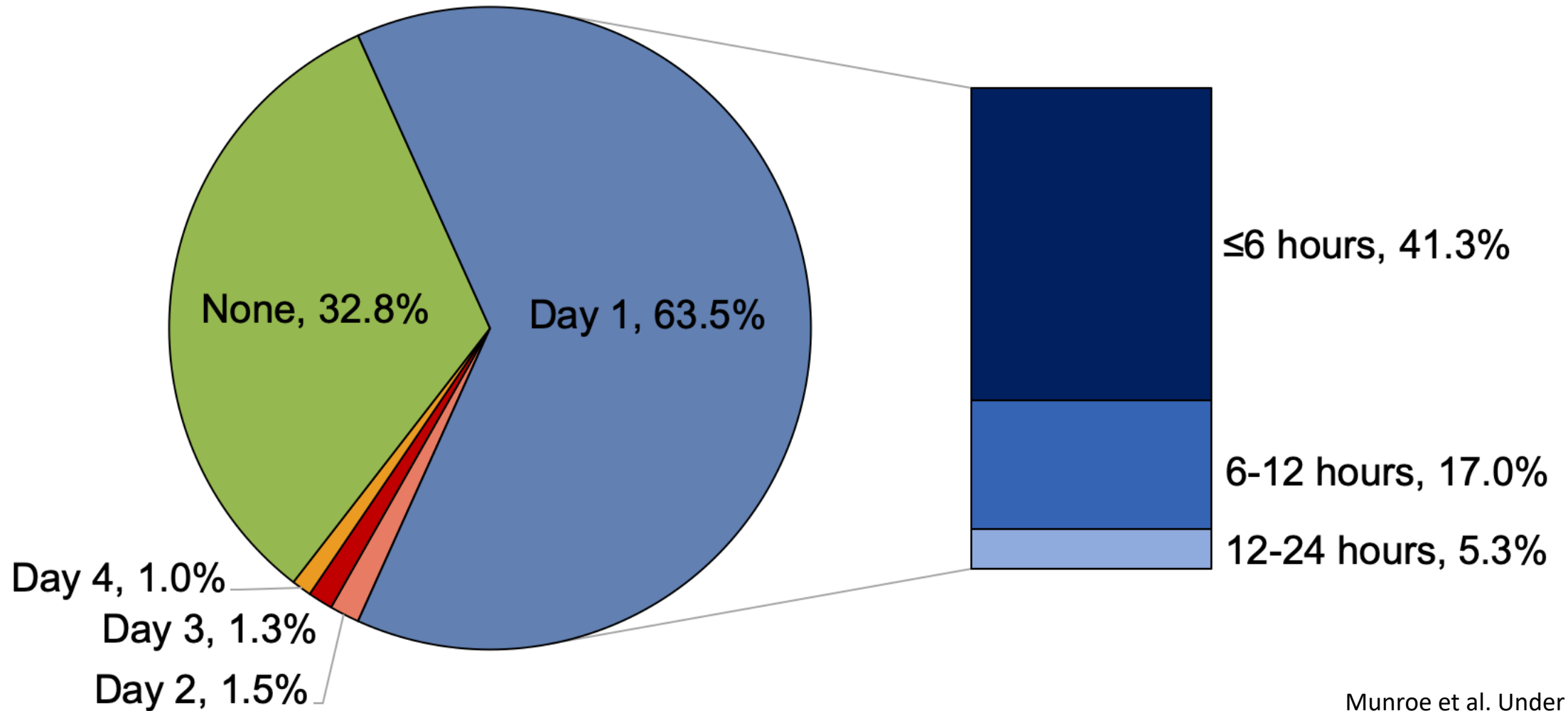


Peripheral initiation was faster

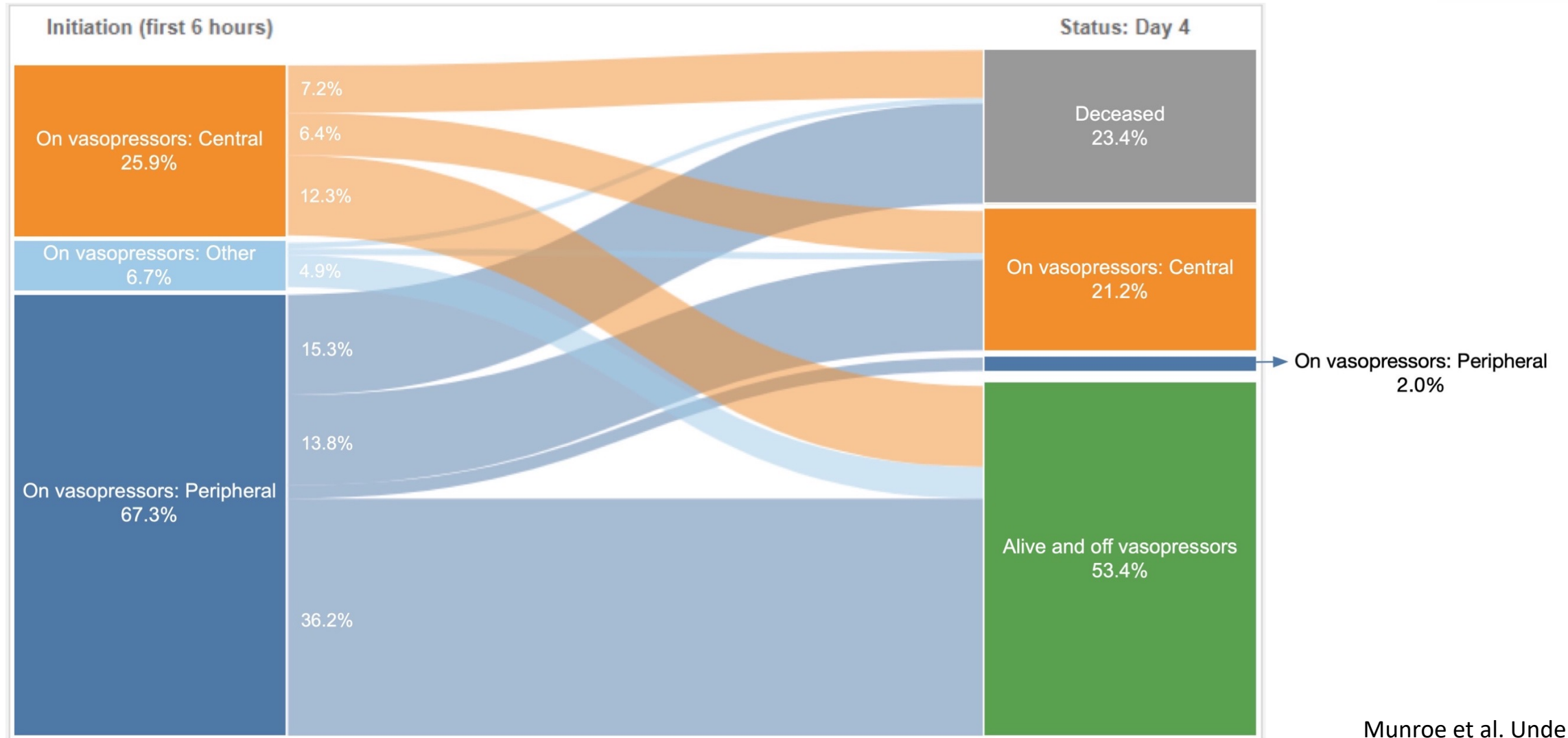


1 in 3 patients avoided a central line

Time to Central Line Placement by day 4 (N=400)



What is happening to these patients?



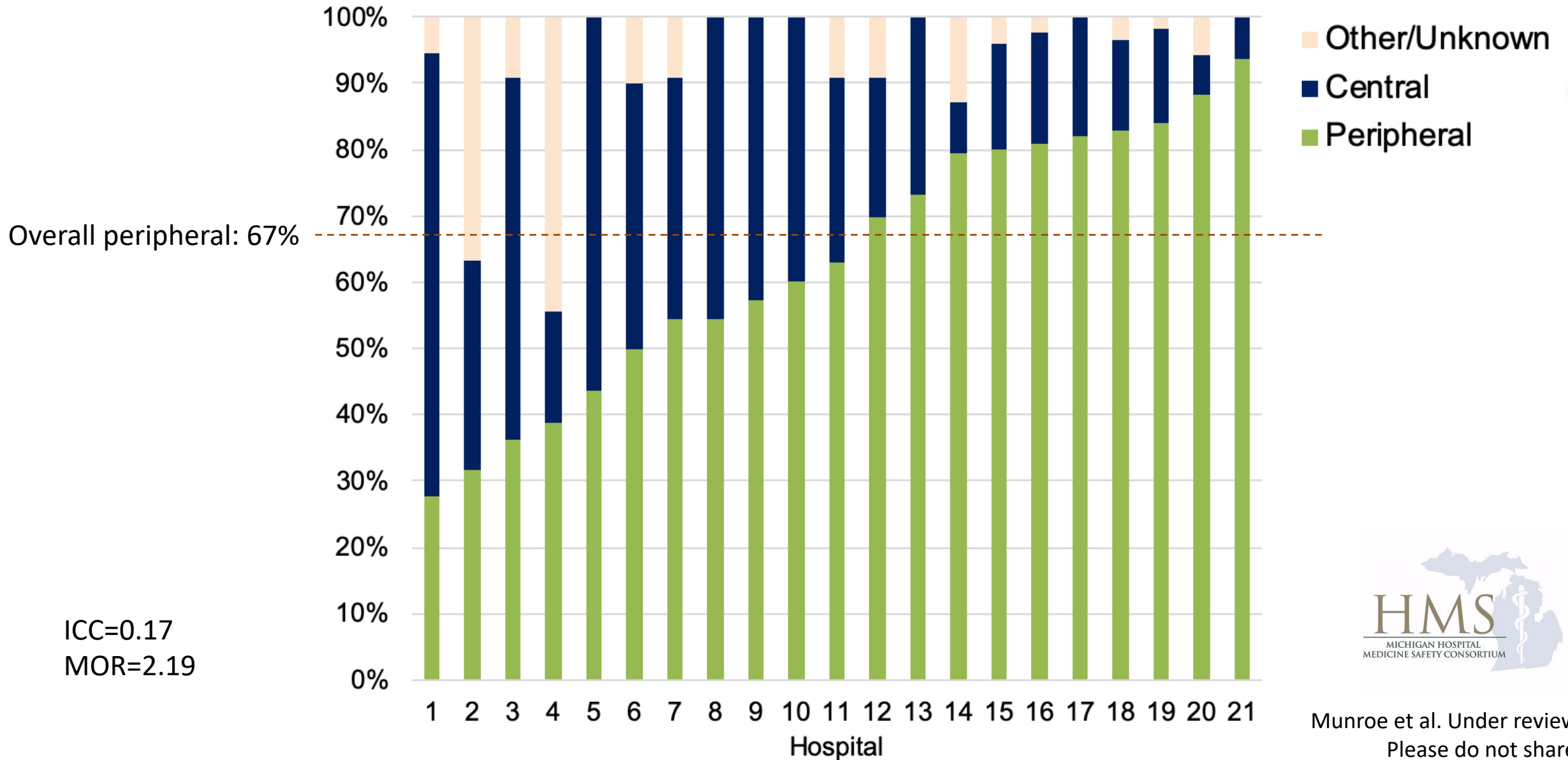
Peripheral: fast, practical, & safe

But, we found a concerning disconnect
between policy and practice

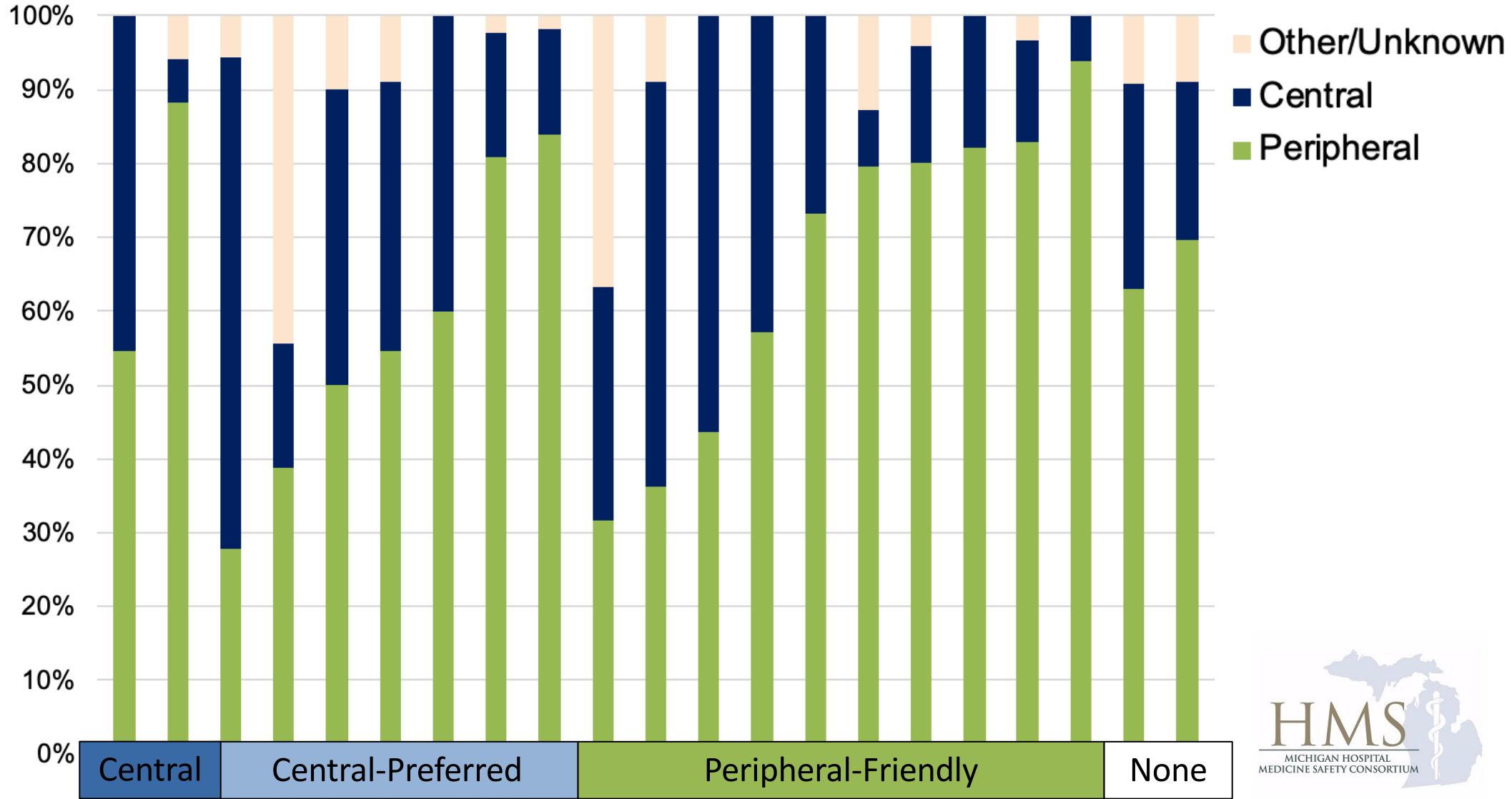
Practice patterns did not match reported policies



Peripheral initiation across Michigan hospitals



Peripheral initiation by hospital policy



Hospital, by policy type



Munroe et al. Under review.
Please do not share.

Peripheral initiation by hospital policy



Hospitals have varying policies.

No relationship to how providers practice.

Hospital, by policy type



Conclusions

- Peripheral vasopressors have **advantages** and are **safe**
- Use varies widely but is very **common**
- Practices don't match policies
- We need to update policies and guidelines to ensure when peripheral vasopressors are used, they are used safely
 - **Monitoring and extravasation management plans** are key

Alternative Options: Midline Catheters?

- 297 midlines vs 1660 PICCs used for vasopressors
- No difference in catheter-related complications
- Increased rate of any blood clots in midlines that needs further evaluation



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Thank you

Questions?