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Impact of body weight on hemodynamic response to fixed dose vasopressin in septic shock

Corissa Piatka

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Impact of Body Weight on Hemodynamic Response to Fixed Dose Vasopressin in Septic Shock

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

Sepsis and Septic Shock

- Sepsis: uncontrolled inflammatory response secondary to infection
  - Hypotension
  - Acute end organ damage
- Common causes of morbidity and mortality in critically ill
  - Mortality rate for septic shock: 40%

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Rhodes A et al. Crit Care Med. 2017 Mar;45(3):486-552.

Sepsis and Septic Shock

Fluid Resuscitation

Broad Spectrum Antibiotics

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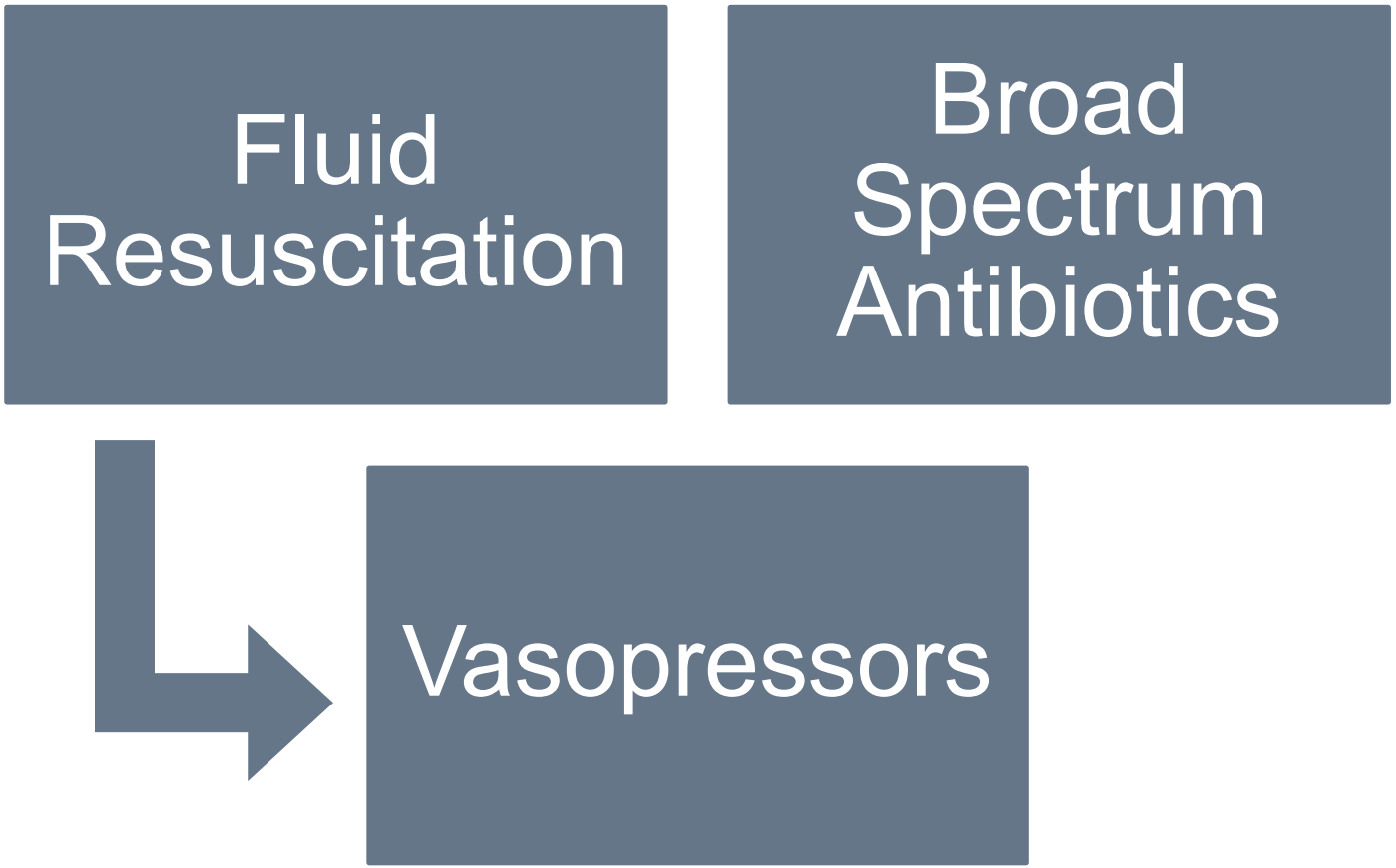
Rhodes A et al. Crit Care Med. 2017 Mar;45(3):486-552.

Sepsis and Septic Shock



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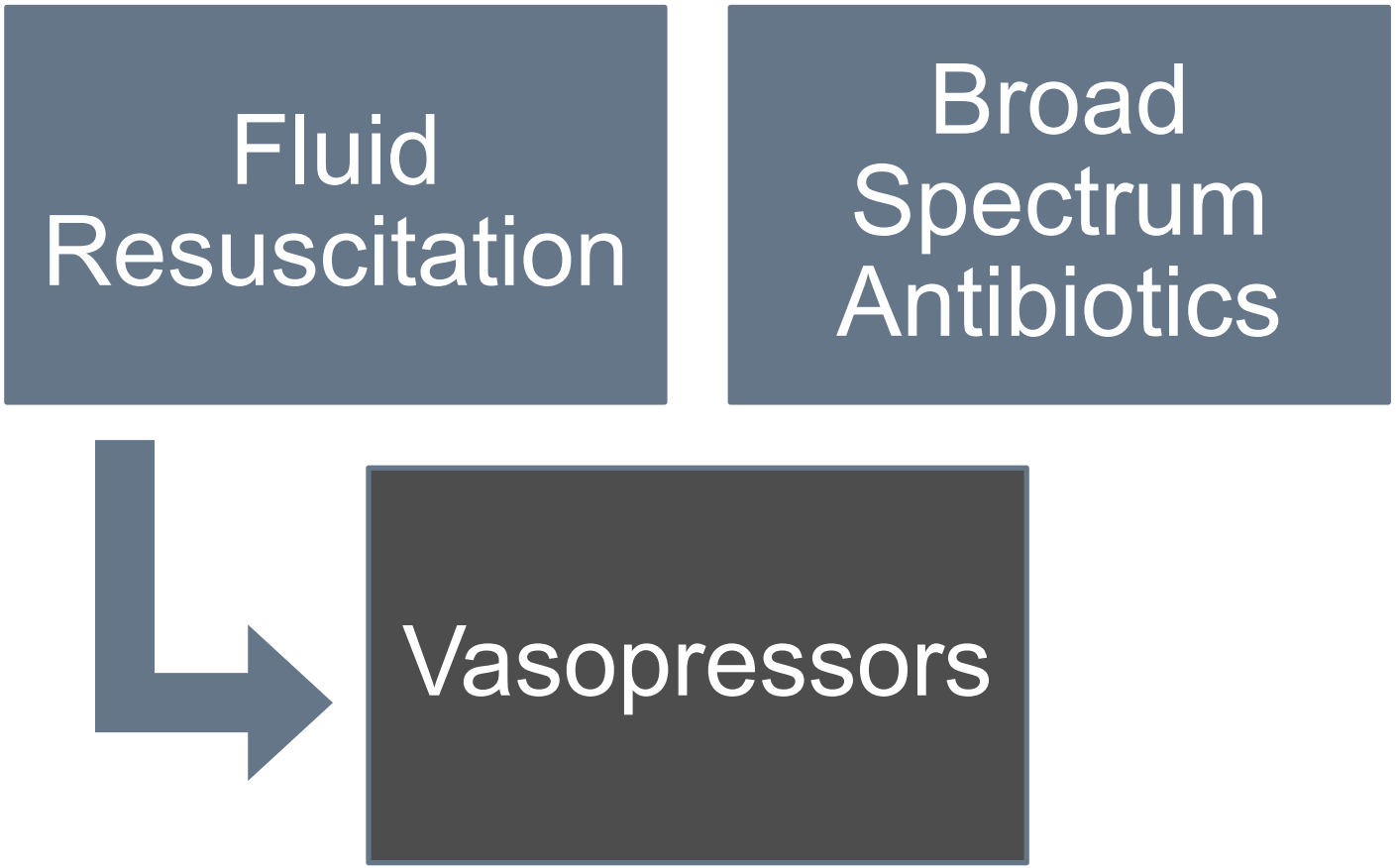
Sepsis and Septic Shock



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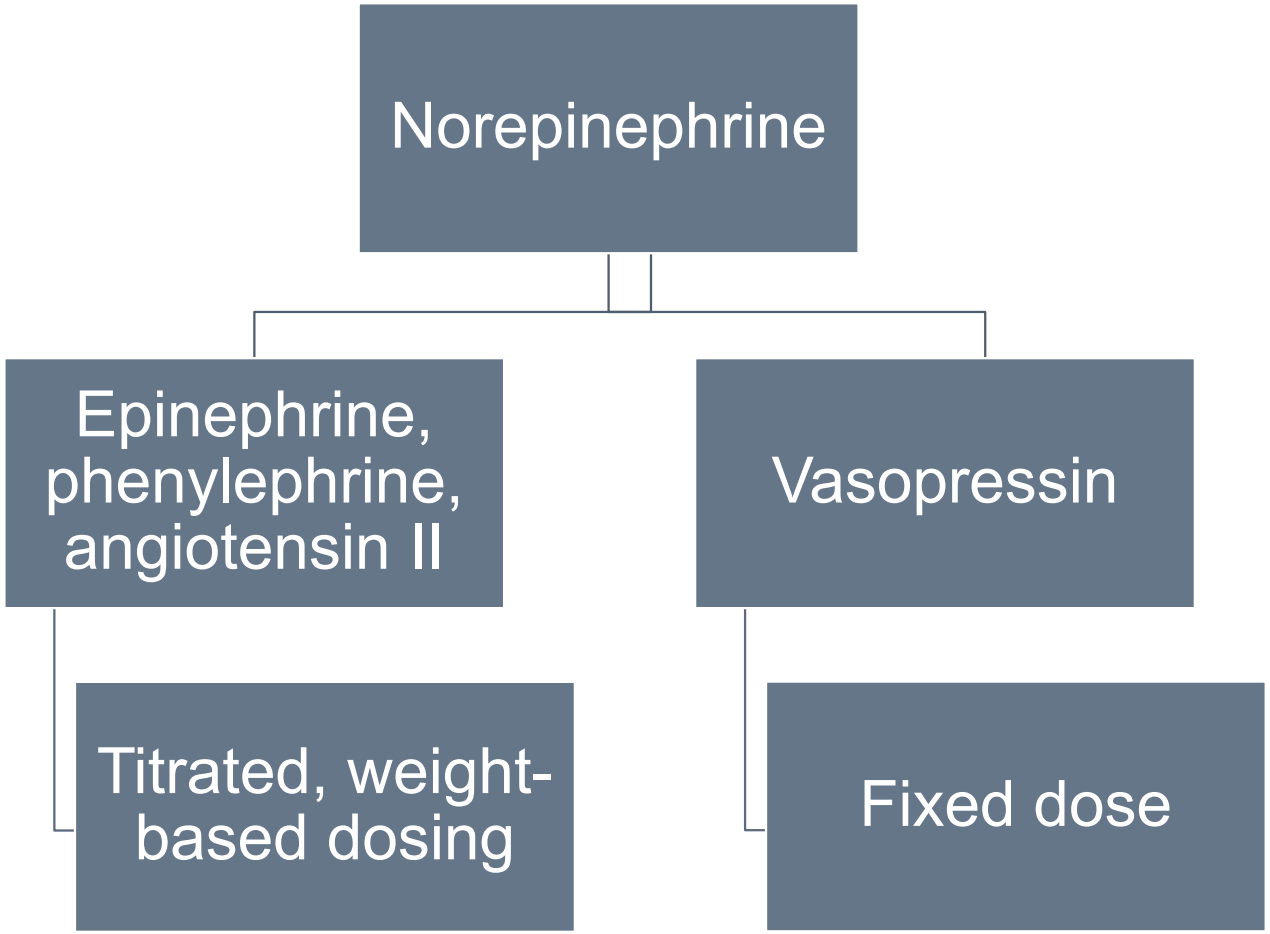

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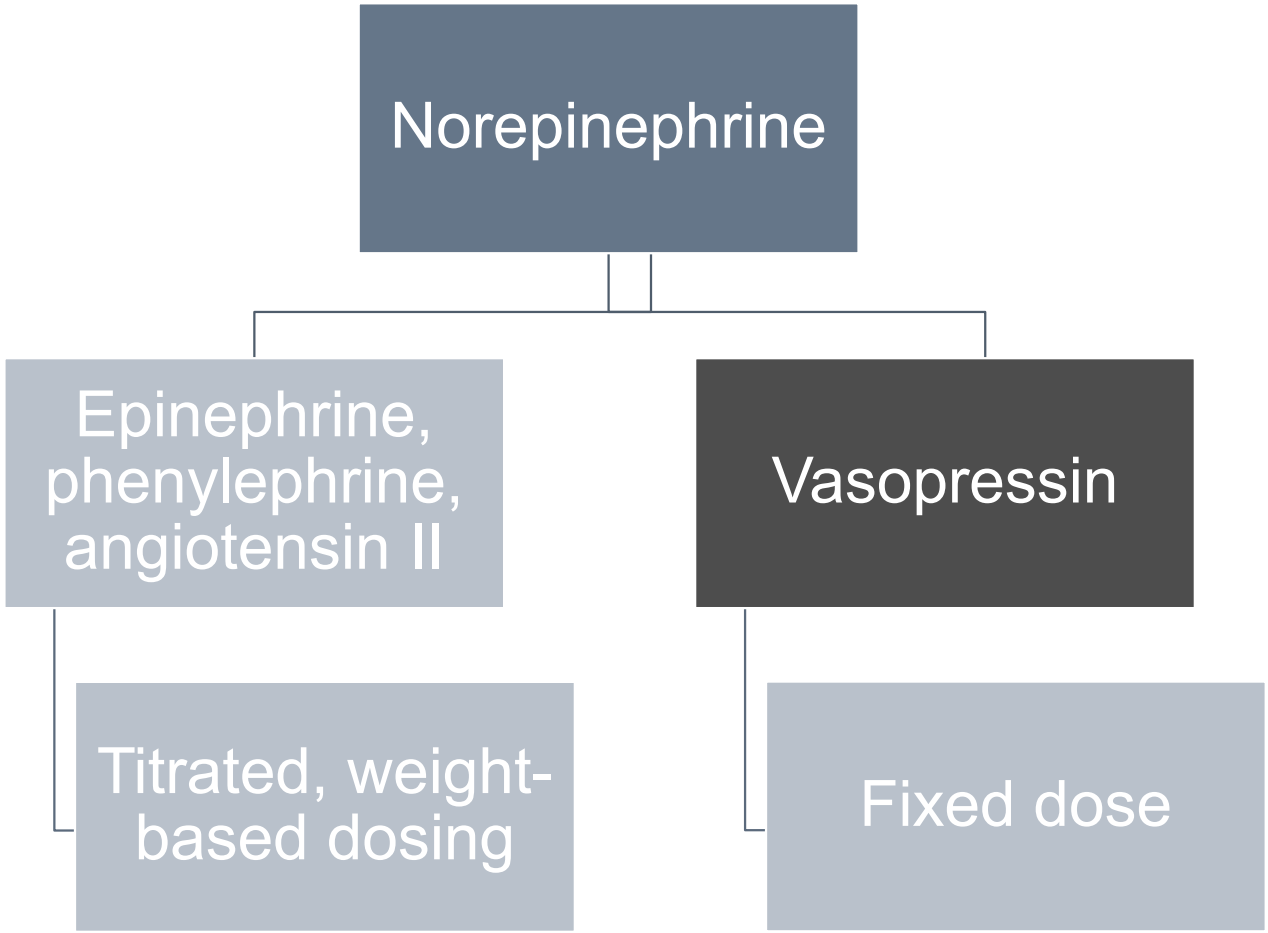

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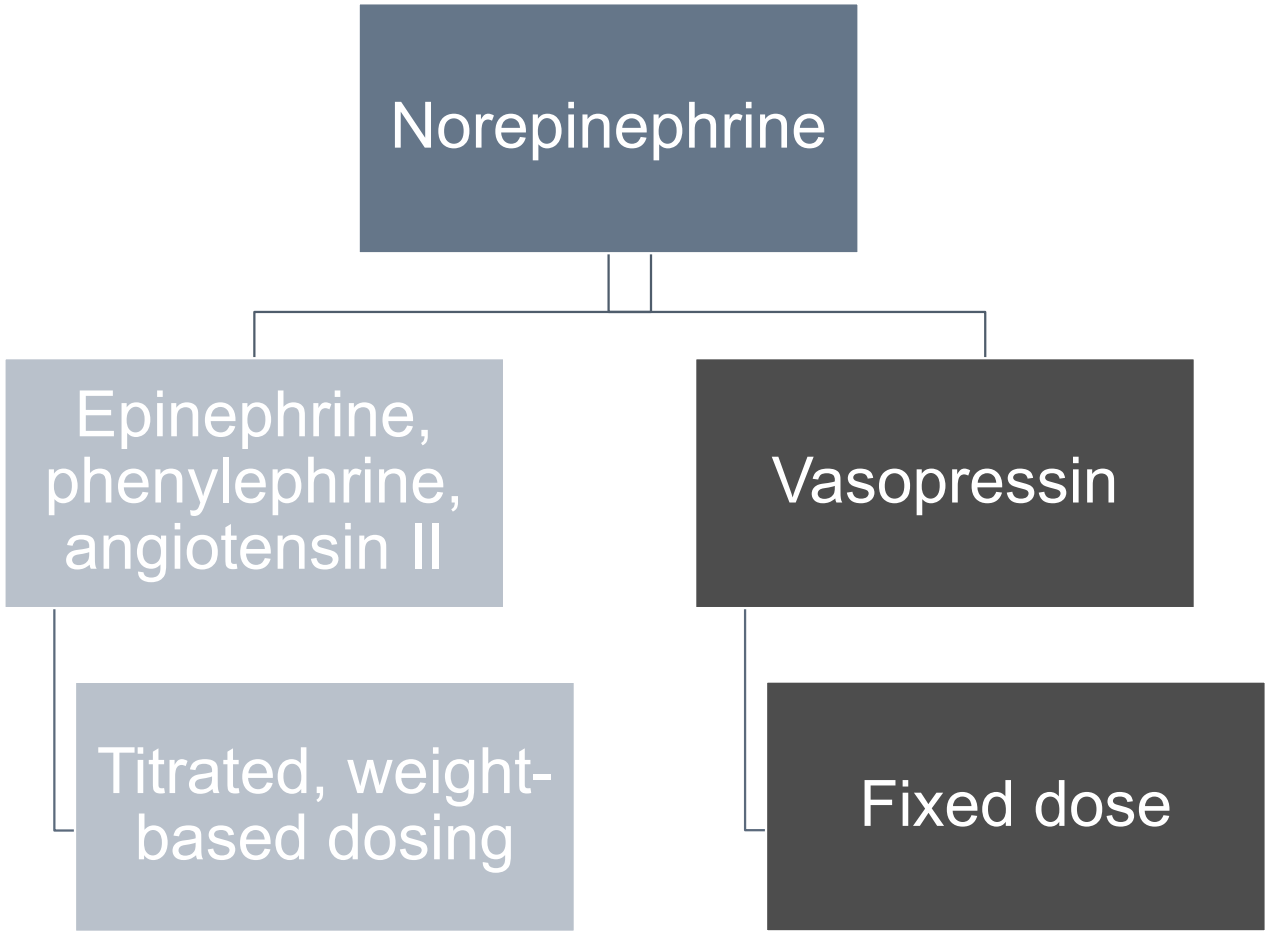

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Rhodes A et al. Crit Care Med. 2017 Mar;45(3):486-552.

Assessment Question #1

Based on administration, how does vasopressin differ from other vasopressors?

A. Vasopressin is titrated; other vasopressors are administered at a flat rate.
B. Vasopressin is administered at a flat rate; other vasopressors are titrated.
C. Vasopressin is administered based on weight; other vasopressors are titrated.
D. Vasopressin is administered based on weight; other vasopressors are administered at a flat rate.

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Assessment Question #2

Which of the following is most likely to occur as a result of vasopressin use in septic shock?

A. Decreased catecholamine requirements
B. Increased cardiac output
C. Renal protective effects
D. Decreased corticosteroid requirements

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Assessment Question #2

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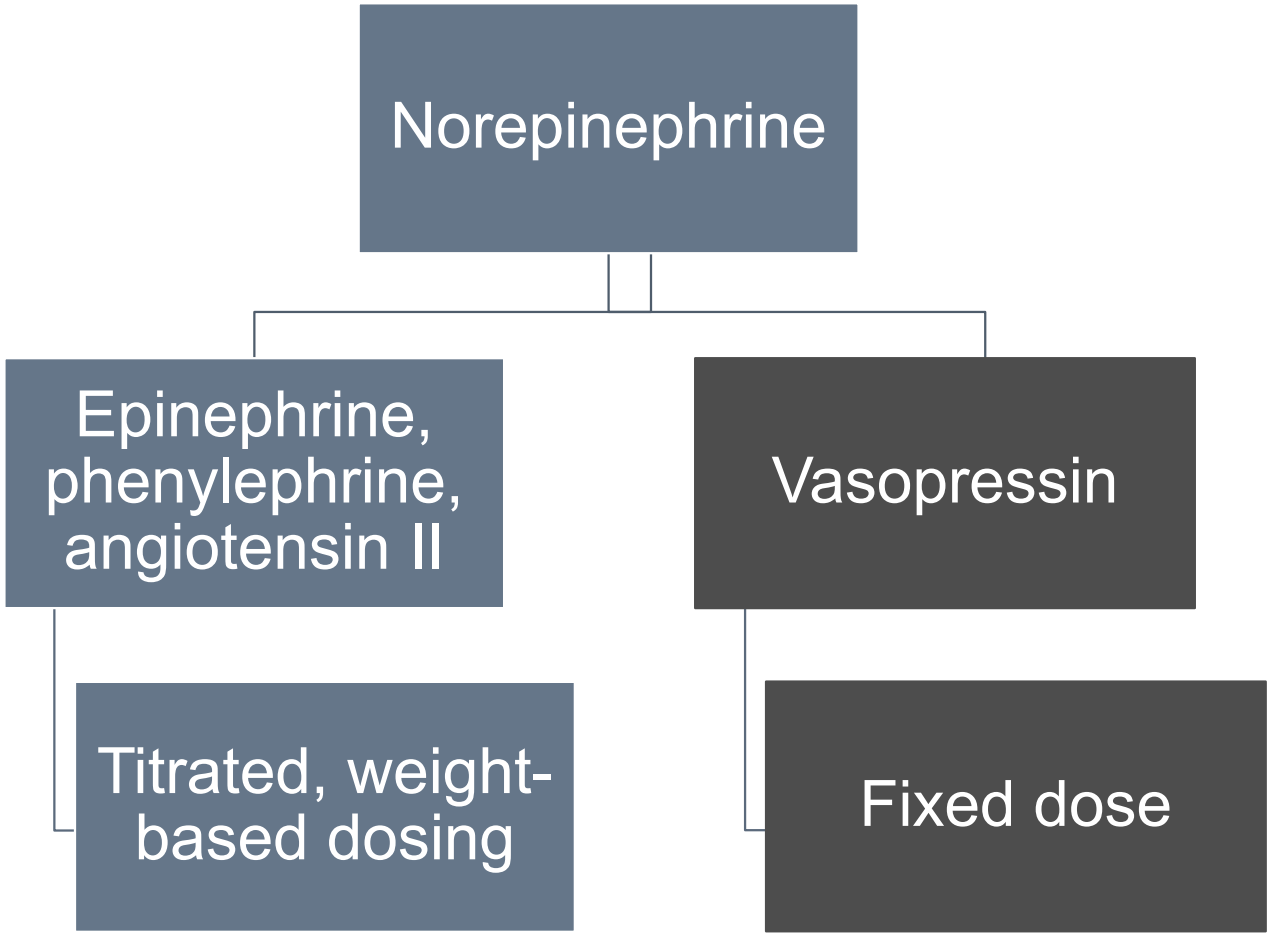
Sepsis and Septic Shock



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Rhodes A et al. Crit Care Med. 2017 Mar;45(3):486-552.

Previous Studies

	Miller et al	Hodge et al
Study Design	Retrospective cohort	Retrospective cohort
Primary Endpoint	Relationship of change in catecholamine vasopressor requirements and vasopressin dosing adjusted for body weight	Change in mean arterial pressure 1 hour after vasopressin initiation relative to body weight
Results	2 hours: r= −0.36, P = 0.03 4 hours: r= −0.46, P < 0.001	Change at 1 hour: r = −0.071 P = 0.84

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Miller JT et al. J Crit Care. 2012 Jun;27(3):289-93.
Hodge EK et al. Ann Pharmacother. 2016 Oct;50(10):816-23.

Previous Studies

- Torbic et al.
  - Single center, retrospective cohort study of patients with septic shock receiving adjunctive fixed dose vasopressin
  - Primary outcome: association between a weight- or a BMI-adjusted vasopressin dose with a catecholamine-dose change or change in mean arterial pressure

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Torbic et al. Shock. 2018;50(4):388-394.

Previous Studies

- Torbic et al.

	BMI < 25 kg/m^2 (n=238)	BMI 25-30 kg/m^2 (n=254)	BMI 30-35 kg/m^2 (n=182)	BMI >35 kg/m^2 (n=264)
Age (years)	62.6 (50.9-71.8)	63.9 (54.6-72.5)	63.3 (53.8-72.1)	60.0 (50.8-69.0)
Male, n (%)	132 (55)	106 (42)	78 (43)	155 (59)
Weight (kg)	62.6 (53.6-70.8)	80.0 (72.0-88.3)	94.3 (84.6-104.5)	122.3 (106.0-140.9)
AVP dose, weight-adjusted (units/kg/min)	0.00049 (0.00042-0.00059)	0.00038 (0.00034-0.00043)	0.00033 (0.00028-0.00038)	0.00026 (0.00022-0.00031)
SOFA score at AVP initiation	12.5 (10-15)	13 (10-16)	13 (11-15)	12 (10-15)
Norepinephrine dose at AVP initiation (mcg/min)	22.3 (18-32)	22 (16-35)	24.5 (18-35)	23.7 (18-33.5)

Results presented as median (IQR) unless otherwise specified.
AVP= vasopressin

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Torbic et al. Shock. 2018;50(4):388-394.

Previous Studies

- Torbic et al.
  - Results: Weight-adjusted

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Previous Studies

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Catecholamine Dose Change

	Vasopressin Dose (units/kg/min)	P-value
2 hours	r = -0.0523 (-0.111 to 0.016)	0.13
6 hours	r = -0.0590 (-0.111 to 0.020)	0.09
12 hours	r = 0.0011 (-0.066 to 0.077)	0.98

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Torbic et al. Shock. 2018;50(4):388-394.

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MAP Change

	Vasopressin Dose (units/kg/min)	P-value
2 hours	r = 0.0356 (-0.215 to 0.111)	0.31
6 hours	r = 0.0481 (-0.033 to 0.092)	0.17
12 hours	r = -0.0146 (-0.115 to 0.016)	0.68

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Torbic et al. Shock. 2018;50(4):388-394.

Previous Studies

- Torbic et al.
  - Results: BMI-adjusted

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Torbic et al. Shock. 2018;50(4):388-394.

Previous Studies

- Torbic et al.
  - Results: BMI-adjusted

Catecholamine Dose Change

	Vasopressin Dose (units/BMI/min)	P-value
2 hours	r = -0.0385 (-0.111 to 0.021)	0.27
6 hours	r = -0.0594 (-0.124 to 0.009)	0.09
12 hours	r = -0.0071 (-0.075 to 0.068)	0.84

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Torbic et al. Shock. 2018;50(4):388-394.

Previous Studies

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12 hours	r = -0.0071 (-0.075 to 0.068)	0.84

MAP Change

	Vasopressin Dose (units/BMI/min)	P-value
2 hours	r = 0.0515 (0.008 to 0.130)	0.14
6 hours	r = 0.0404 (-0.029 to 0.099)	0.09
12 hours	r = -0.0056 (-0.091 to 0.041)	0.87

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Torbic et al. Shock. 2018;50(4):388-394.

Purpose

- Evaluate effect of body weight on achievement of target mean arterial pressure (MAP) post-initiation of vasopressin in patients with septic shock

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Parkview Regional Medical Center

- Parkview Health
- Community hospital
- Level II trauma center
- 460 adult and pediatric inpatient beds
- 6 critical care units
  - Medical ICU (MICU)
  - Surgical Trauma ICU (STICU)
  - Cardiovascular ICU (CVICU)

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Parkview Regional Medical Center

- Vasopressor Use
  - Provider preference
    - Norepinephrine
      - Titrated 2-30 mcg/min
      - Titrated 2-50 mcg/min
    - Vasopressin
      - Continuous at 0.03 units/hr
      - Continuous at 0.04 units/hr

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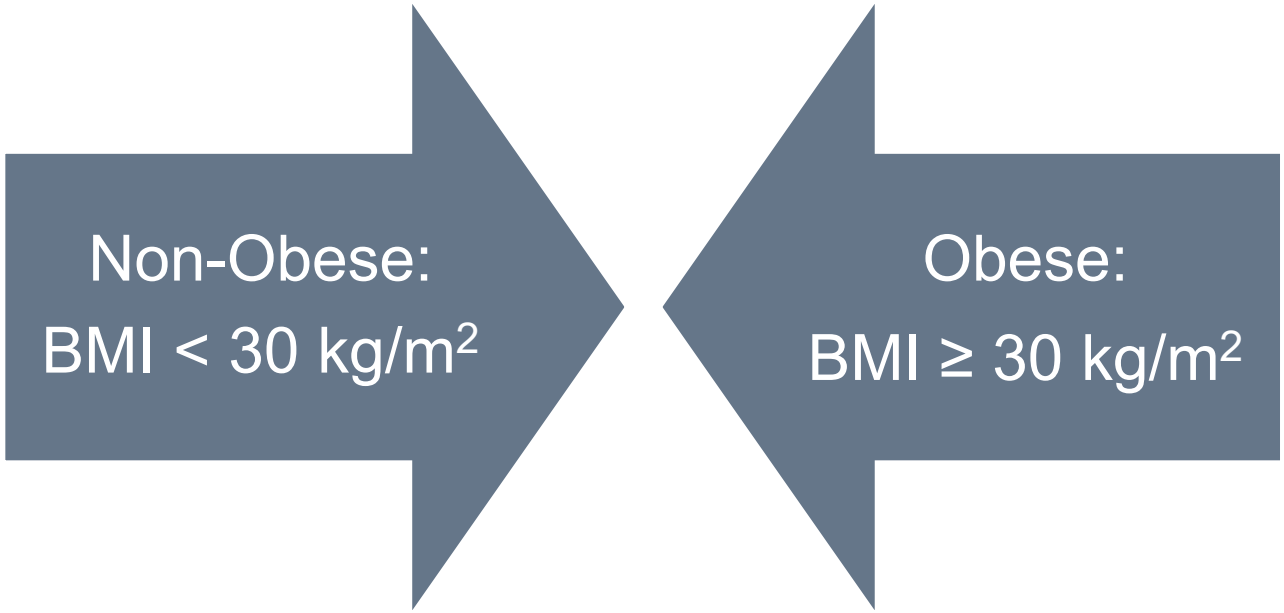
Study Design

- Single center
- Retrospective, electronic chart review
- Patients admitted March 2017 through August 2018



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BMI = Body Mass Index

Inclusion and Exclusion Criteria

Inclusion

- Age ≥18 years
- Diagnosis of sepsis or septic shock per ICD 10 code
- Admitted to MICU, STICU, CVICU
- Initiated on catecholamine infusion prior to vasopressin infusion

Exclusion

- Age <18 years
- Indication other than septic shock
- Vasopressin monotherapy
- Catecholamine or vasopressin infusion duration < 1 hour
- Baseline MAP ≥ 65 mmHg at vasopressin initiation
- Transfer from outside ICU

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Primary Outcome

- Achievement of target MAP within 4 hours of vasopressin initiation

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Definition of Target MAP

Hammond DA et al. J Intensive Care Med. 2017 Jan 1:885066617725255.

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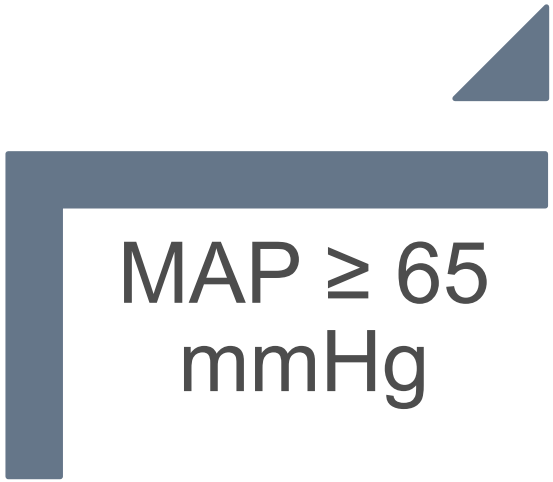
Definition of Target MAP



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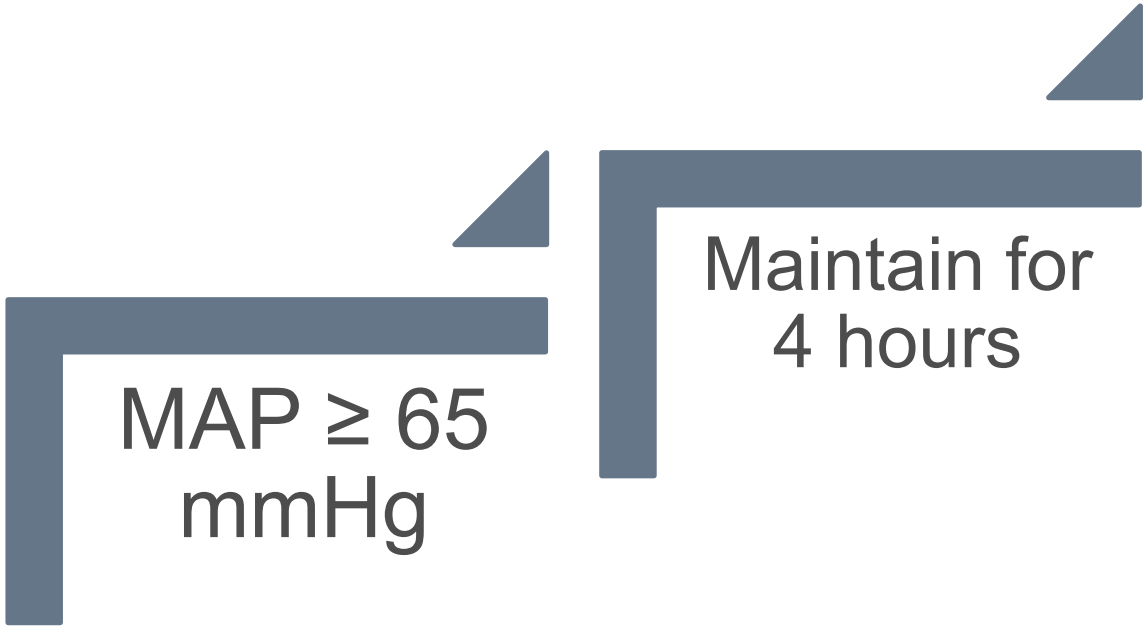
Definition of Target MAP



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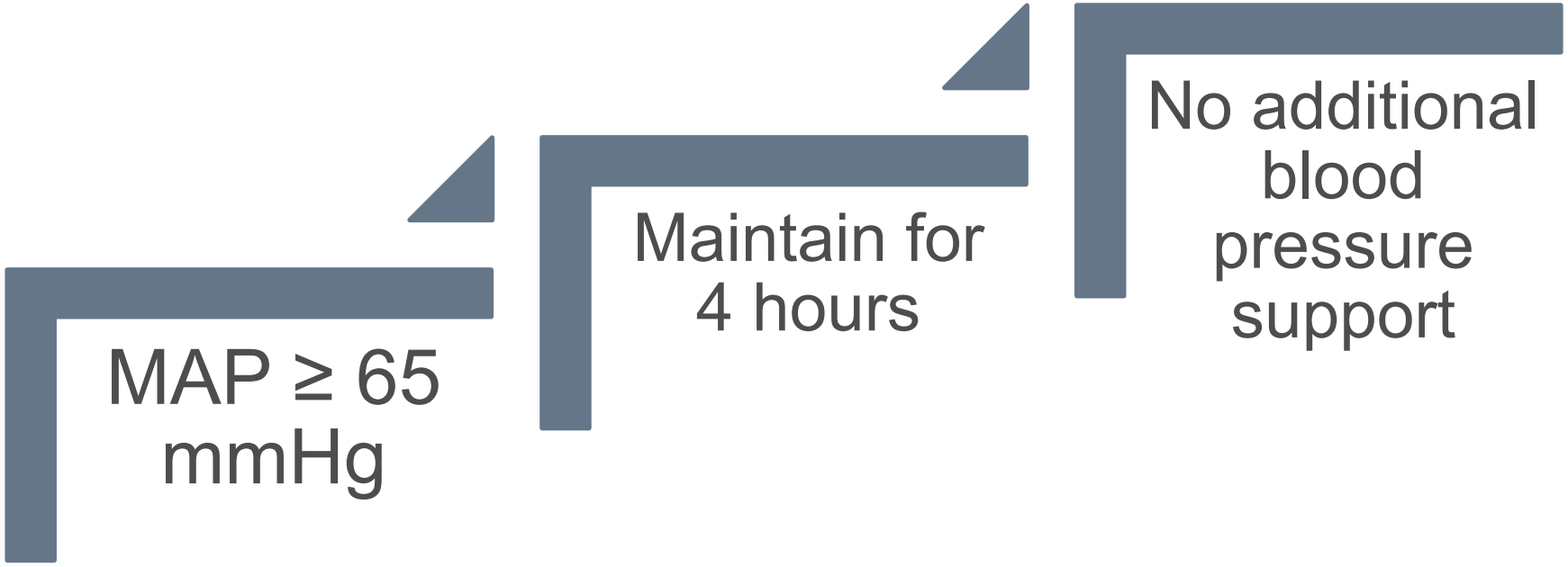

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Secondary Outcomes

- Change in MAP at 4 hours after vasopressin initiation
- Total norepinephrine infusion duration
- Intensive care unit length of stay
- Hospital length of stay
- In-hospital mortality

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Statistical Tests

- 324 patients (162 per study arm) for 80% power
  - 15% difference in target MAP achievement
  - A priori α error rate: 0.05

Primary Outcome	Secondary Outcomes
• Chi-square test	• Mann-Whitney rank sum • Chi-square test

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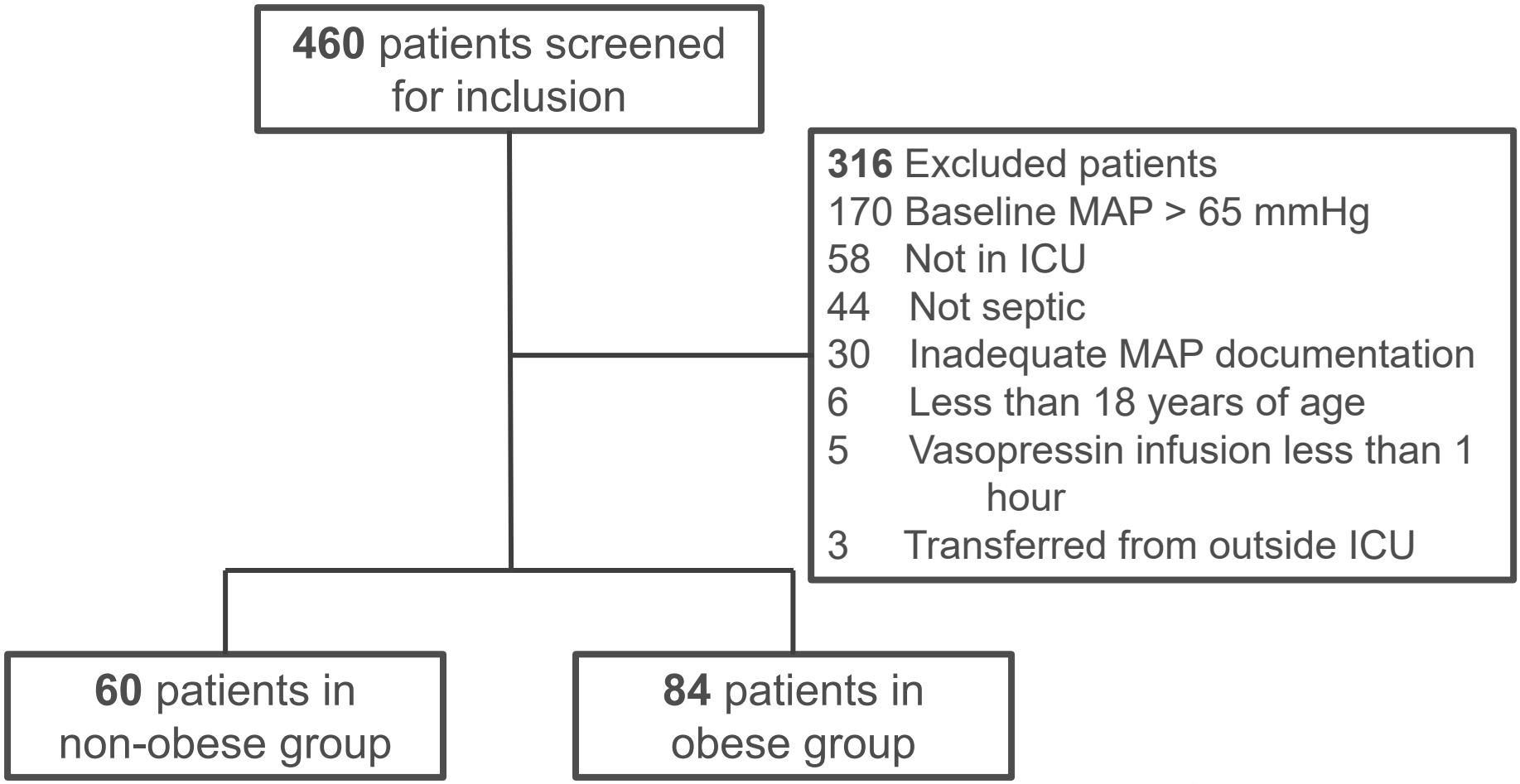
Study Population



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Results: Baseline Characteristics

	Non-Obese (n=60)	Obese (n=84)
Age (years)	69 (61-77)	65 (58-72)
Male, n (%)	35 (58)	39 (46)
Weight (kg)	72.4 (62.3-82.6)	104.7 (92.8-121.9)
Body mass index (kg/m^2)	25.0 (21.9-27.5)	37.9 (33.0-44.9)
AVP dose, weight-adjusted (units/kg/min)	0.000515 (0.00043-0.000577)	0.00033 (0.00027-0.000408)
SOFA score at AVP initiation	11 (9-13)	12 (9-13)
Norepinephrine equivalent dose at AVP initiation (mcg/min)	26.5 (20-30)	26 (22-30)
Norepinephrine duration at AVP initiation (hours)	7.0 (3.8-17.5)	7.2 (3.4-31.5)
MAP at AVP initation (mmHg)	58 (52-60)	56 (50-60)

Results presented as median (IQR) unless otherwise specified.
AVP= vasopressin

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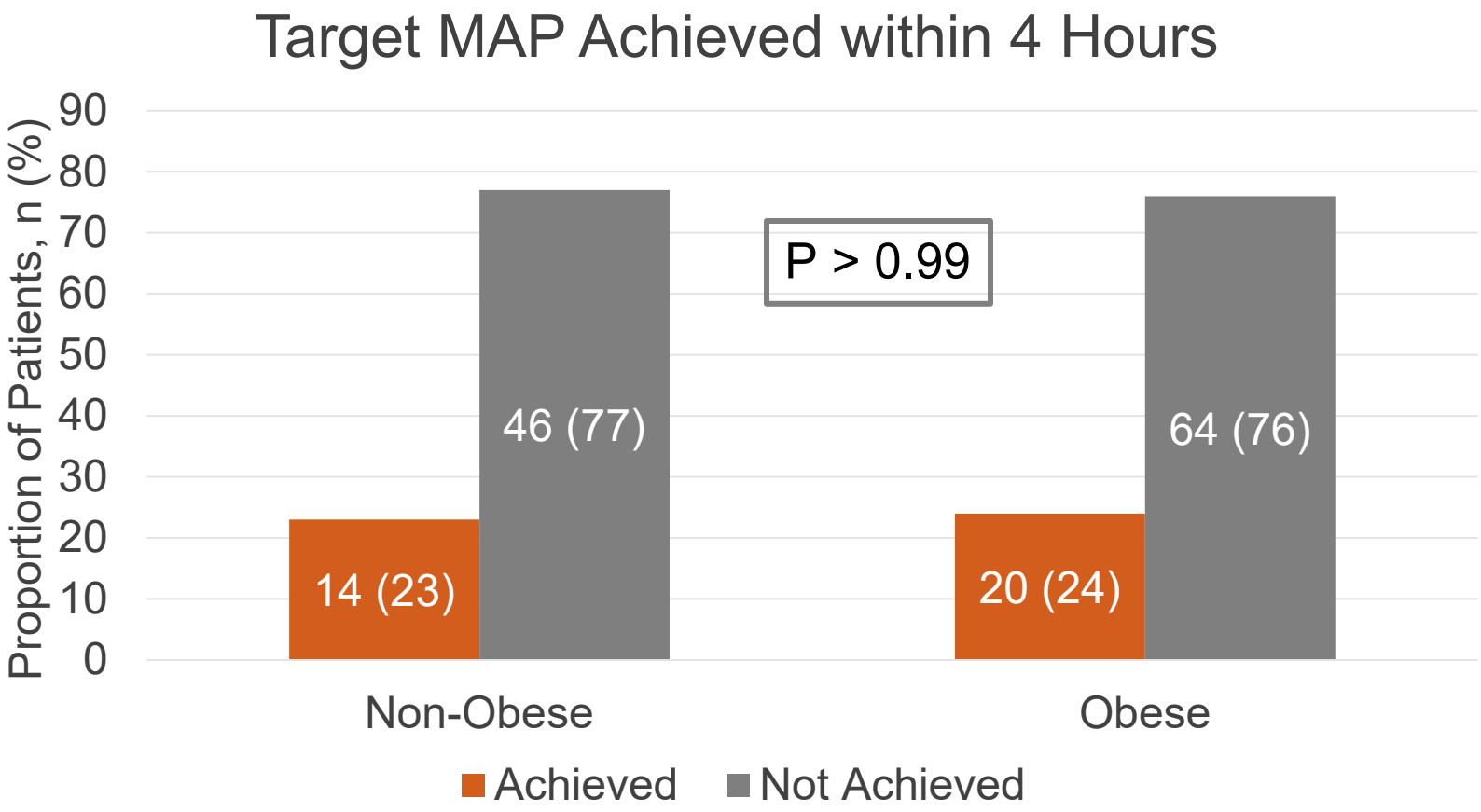
Results: Primary Outcome



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Results: Secondary Outcomes

	Non-Obese (n=60)	Obese (n=84)	P-value
Change in MAP at 4 hours (mmHg), median (IQR)	8 (2-18)	12 (4-19)	0.467
Norepinephrine infusion duration (hours), median (IQR)	80.2 (50.5-134.6)	119.8 (64.0-181.7)	0.018
ICU length of stay (days), median (IQR)	5.8 (2.1-10.4)	6.6 (3.3-12.2)	0.159
Hosptial length of stay (days), median (IQR)	8.2 (3.6-16.9)	8.3 (5.8-18.7)	0.477
In-hospital mortality, n (%)	26 (43)	44 (52)	0.367

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Discussion

- Body weight did not impact the achievement of target MAP
  - Consistent with current literature
  - Lack of power

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Limitations

- Single center
- Retrospective chart review
  - MAP documentation
    - Timing
    - Arterial line versus cuff
  - Infusion documentation
    - End time accuracy
- BMI criteria
- Mean arterial pressure target as primary outcome
- Strict definition of target MAP

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Future Directions

- Redesign to increase patient population
  - Expansion of MICU and intensive care step-down unit
- Evaluation of vasopressin role in septic shock
- Publication

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Acknowledgements

- Michael E Todt, PharmD, BCCCP
- Dustin D Linn, PharmD, BCPS, BCCCP
- Sarah Ferrell, PharmD
- Robert Beckett, PharmD, BCPS

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