

## Supplement 1: Search Strategy

**5.5.20 PubMed (245)** (((("Vasoplegia"[Mesh]) OR vasoplegic syndrome) OR vasoplegic shock) OR vasopleg\* [tiab])) AND

((((((((norepinephrine) OR methylene blue) OR vitamin b12) OR epinephrine)) OR vasopressin)) OR

((((((((norepinephrine) OR methylene blue) OR vitamin b12) OR epinephrine)) AND vasopressin))

Filters: English

((("Vasoplegia"[MeSH Terms] OR ((("Vasoplegia"[MeSH Terms] OR "Vasoplegia"[All Fields]) OR ("vasoplegic"[All Fields] AND "syndrome"[All Fields])) OR "vasoplegic syndrome"[All Fields])) OR ("vasoplegic"[All Fields] AND (((("shock"[MeSH Terms] OR "shock"[All Fields]) OR "shocked"[All Fields]) OR "shocking"[All Fields]) OR "shocks"[All Fields]))) OR "vasopleg\*" [Title/Abstract]) AND (((((((((((("noradrenaline s"[All Fields] OR "norepinephrin"[All Fields]) OR "norepinephrine"[MeSH Terms]) OR "norepinephrine"[All Fields]) OR "noradrenalin"[All Fields]) OR "noradrenaline"[All Fields]) OR "norepinephrines"[All Fields]) OR (("methylene blue"[MeSH Terms] OR ("methylene"[All Fields] AND "blue"[All Fields])) OR "methylene blue"[All Fields])) OR (((("vitamin b 12"[MeSH Terms] OR "vitamin b 12"[All Fields]) OR ("vitamin"[All Fields] AND "b12"[All Fields])) OR "vitamin b12"[All Fields])) OR (((("epinephrine"[MeSH Terms] OR "epinephrine"[All Fields]) OR "adrenalin"[All Fields]) OR "adrenaline"[All Fields]) OR "epinephrin"[All Fields]) OR "epinephrines"[All Fields])) OR (((("vasopressin s"[All Fields] OR "vasopressine"[All Fields]) OR "vasopressins"[MeSH Terms]) OR "vasopressins"[All Fields]) OR "vasopressin"[All Fields])) OR (((((((((((("noradrenaline s"[All Fields] OR "norepinephrin"[All Fields]) OR "norepinephrine"[MeSH Terms]) OR "norepinephrine"[All Fields]) OR "noradrenalin"[All Fields]) OR "noradrenaline"[All Fields]) OR "norepinephrines"[All Fields]) OR (("methylene blue"[MeSH Terms] OR ("methylene"[All Fields] AND "blue"[All Fields])) OR "methylene blue"[All Fields])) OR (((("vitamin b 12"[MeSH Terms] OR "vitamin b 12"[All Fields]) OR ("vitamin"[All Fields] AND "b12"[All Fields])) OR "vitamin b12"[All Fields])) OR (((("epinephrine"[MeSH Terms] OR "epinephrine"[All Fields]) OR "adrenalin"[All Fields]) OR "adrenaline"[All Fields]) OR "epinephrin"[All Fields]) OR "epinephrines"[All Fields])) AND (((("vasopressin s"[All Fields] OR "vasopressine"[All Fields]) OR "vasopressins"[MeSH Terms]) OR "vasopressins"[All Fields]) OR "vasopressin"[All Fields]))))

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### Translations

**vasoplegic syndrome:** "vasoplegia"[MeSH Terms] OR "vasoplegia"[All Fields] OR ("vasoplegic"[All Fields] AND "syndrome"[All Fields]) OR "vasoplegic syndrome"[All Fields]

**shock:** "shock"[MeSH Terms] OR "shock"[All Fields] OR "shocked"[All Fields] OR "shocking"[All Fields] OR "shocks"[All Fields]

**norepinephrine:** "noradrenaline's"[All Fields] OR "norepinephrin"[All Fields] OR "norepinephrine"[MeSH Terms] OR "norepinephrine"[All Fields] OR "noradrenalin"[All Fields] OR "noradrenaline"[All Fields] OR "norepinephrines"[All Fields]

**methylene blue:** "methylene blue"[MeSH Terms] OR ("methylene"[All Fields] AND

"blue"[All Fields]) OR "methylene blue"[All Fields]  
**vitamin b12:** "vitamin b 12"[MeSH Terms] OR "vitamin b 12"[All Fields] OR ("vitamin"[All Fields] AND "b12"[All Fields]) OR "vitamin b12"[All Fields]  
**epinephrine:** "epinephrine"[MeSH Terms] OR "epinephrine"[All Fields] OR "adrenalin"[All Fields] OR "adrenaline"[All Fields] OR "epinephrin"[All Fields] OR "epinephrines"[All Fields]  
**vasopressin:** "vasopressin's"[All Fields] OR "vasopressine"[All Fields] OR "vasopressins"[MeSH Terms] OR "vasopressins"[All Fields] OR "vasopressin"[All Fields]  
**norepinephrine:** "noradrenaline's"[All Fields] OR "norepinephrin"[All Fields] OR "norepinephrine"[MeSH Terms] OR "norepinephrine"[All Fields] OR "noradrenalin"[All Fields] OR "noradrenaline"[All Fields] OR "norepinephrines"[All Fields]  
**methylene blue:** "methylene blue"[MeSH Terms] OR ("methylene"[All Fields] AND "blue"[All Fields]) OR "methylene blue"[All Fields]  
**vitamin b12:** "vitamin b 12"[MeSH Terms] OR "vitamin b 12"[All Fields] OR ("vitamin"[All Fields] AND "b12"[All Fields]) OR "vitamin b12"[All Fields]  
**epinephrine:** "epinephrine"[MeSH Terms] OR "epinephrine"[All Fields] OR "adrenalin"[All Fields] OR "adrenaline"[All Fields] OR "epinephrin"[All Fields] OR "epinephrines"[All Fields]  
**vasopressin:** "vasopressin's"[All Fields] OR "vasopressine"[All Fields] OR "vasopressins"[MeSH Terms] OR "vasopressins"[All Fields] OR "vasopressin"[All Fields]

### 5.5.20 Embase <1974 to 2020 May 04> Search Strategy (393)

- 1 vasoplegic syndrome.mp. or exp \*vasoplegia/ (327)
- 2 vasoplegic shock.mp. (135)
- 3 vasopleg\*.ti. or vasopleg\*.ab. (727)
- 4 1 or 2 or 3 (764)
- 5 norepinephrine.mp. or exp noradrenalin/ (140871)
- 6 methylene blue.mp. or exp \*methylene blue/ (24412)
- 7 vitamin b12.mp. or exp \*cyanocobalamin/ (25874)
- 8 exp \*epinephrine/ or epinephrine.mp. (50403)
- 9 exp \*vasopressin/ or vasopressin.mp. (59633)
- 10 5 or 6 or 7 or 8 or 9 (276986)
- 11 5 or 6 or 7 or 8 (224895)
- 12 9 and 11 (7542)
- 13 11 or 12 (224895)
- 14 4 and 13 (419)
- 15 limit 14 to english language (393)

**5.5.20 Scopus (300)** ( ( TITLE-ABS-KEY ( vasoplegia OR "vasoplegic syndrome" OR "vasoplegic shock" ) OR TITLE ( vasopleg\* ) OR ABS ( vasopleg\* ) ) ) AND ( ( TITLE-ABS-KEY ( norepinephrine OR "methylene blue" OR "vitamin b12" OR epinephrine OR vasopressin ) ) OR ( ( TITLE-ABS-KEY ( norepinephrine OR "methylene blue" OR "vitamin b12" OR epinephrine ) AND TITLE-ABS-KEY ( vasopressin ) ) ) ) AND ( LIMIT-TO ( LANGUAGE , "English" ) )

**5.5.20 Web of Science (245)** TOPIC: (norepinephrine OR "methylene blue" OR "vitamin b12" OR epinephrine OR vasopressin) OR TOPIC: (norepinephrine OR "methylene blue" OR "vitamin b12" OR epinephrine) and TOPIC: (vasopressin) AND TOPIC: (vasoplegia OR "vasoplegic syndrome" OR "vasoplegic shock" OR vasopleg\*) Refined by: LANGUAGES: ( ENGLISH )Indexes=SCI-EXPANDED, ESCI Timespan=All years

**5.5.20 EBM Reviews - Cochrane Database of Systematic Reviews <2005 to May 1, 2020> Search Strategy (2)**

- 1 (vasoplegia or "vasoplegic syndrome" or "vasoplegic shock" or vasopleg\*).mp. [mp=title, short title, abstract,full text, keywords, caption text] (2)
- 2 (norepinephrine or "methylene blue" or "vitamin b12" or epinephrine or vasopressin).mp. [mp=title, short title,abstract, full text, keywords, caption text] (541)
- 3 (norepinephrine or "methylene blue" or "vitamin b12" or epinephrine).mp. [mp=title, short title, abstract, full text, keywords, caption text] (481)
- 4 vasopressin.mp. [mp=title, short title, abstract, full text, keywords, caption text] (84)
- 5 3 and 4 (24)
- 6 2 or 5 (541)
- 7 1 and 6 (2)

**4.19.20 Author supplied (3)**

DATABASE	RESULTS	DUPLICATES	REMAINING
PubMed	218	3	215
Embase	393	200	193
Scopus	300	235	65
Web of Science	245	192	53
Cochrane Database of Systematic Reviews	2	0	2
Author Supplied	3	1	2
<b>TOTAL</b>	<b>1161</b>	<b>631</b>	<b>530</b>

## Supplement 2: Certainty of Evidence for Outcomes

### 30-day mortality

Study design (Number of studies)	Number of patients	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Risk ratio	Certainty of evidence
Cohort (1)	338	Not serious	Not Applicable	Not serious	Serious	None	3.33, 95% CI 0.93, 11.90	Very low
RCT (1)	300	Serious	Not Applicable	Not serious	Not serious	None	0.97, 95% CI 0.57, 1.64	Moderate

### Ventricular arrhythmia

Study design (Number of studies)	Number of patients	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Risk ratio	Certainty of evidence
Cohort (1)	338	Not serious	Not Applicable	Not serious	Serious	None	1.75, 95% CI 1.11, 2.76	Very low
RCT (1)	300	Serious	Not Applicable	Not serious	Not serious	None	0.86, 95% CI 0.54, 1.35	Moderate

### **Duration of vasopressors**

Study design (Number of studies)	Number of patients	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Mean difference	Certainty of evidence
Cohort (1)	338	Not serious	Not Applicable	Not serious	Serious	None	24 days, 95% CI 16.32, 31.68	Very low
RCT (1)	300	Serious	Not Applicable	Not serious	Not serious	None	-23.00 days, 95% CI -36.12, -9.88	Moderate

### **Intensive care unit length of stay**

Study design (Number of studies)	Number of patients	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Mean difference	Certainty of evidence
<b>Vasopressin vs Norepinephrine</b>								
Cohort (1)	338	Not serious	Not Applicable	Not serious	Not serious	None	1.00 days, 95% CI 0.53; 1.47	Low
RCT (1)	300	Serious	Not Applicable	Not serious	Not serious	None	-1.00 days, 95% CI -1.69, -0.31	Moderate
<b>Vasopressin vs Methylene blue</b>								
RCT (1)	40	Serious	Not Applicable	Not serious	Very serious	None	1.60 days, 95% CI -0.29, 3.49	Very low

**Stroke**

Study design (Number of studies)	Number of patients	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Risk ratio	Certainty of evidence
Cohort (1)	338	Not serious	Not Applicable	Not serious	Serious	None	0.50, 95% CI 0.13, 1.97	Very low
RCT (1)	300	Serious	Not Applicable	Not serious	Serious	None	1.01, 95% CI 0.26, 3.98	Low

**Acute kidney injury stage II/III**

Study design (Number of studies)	Number of patients	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Risk ratio	Certainty of evidence
Cohort (1)	338	Not serious	Not Applicable	Not serious	Serious	None	1.12, 95% CI 0.89, 1.42	Very low
RCT (1)	300	Serious	Not Applicable	Not serious	Not serious	None	0.32, 95% CI 0.21, 0.49	Moderate

### **Atrial fibrillation**

Study design (Number of studies)	Number of patients	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Risk ratio	Certainty of evidence
Cohort (1)	338	Not serious	Not Applicable	Not serious	Not serious	None	1.70, 95% CI 1.02, 2.83	Low
RCT (1)	300	Serious	Not Applicable	Not serious	Not serious	None	0.78, 95% CI 0.67, 0.89	Moderate

### **Mechanical ventilation > 48 hours**

Study design (Number of studies)	Number of patients	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Risk ratio	Certainty of evidence
Cohort (1)	338	Not serious	Not Applicable	Not serious	Serious	None	0.95, 95% CI 0.63, 1.42	Very low
RCT (1)	300	Serious	Not Applicable	Not serious	Serious	None	0.62, 95% CI 0.27, 1.46	Low

CI: Confidence interval, RCT: Randomized controlled trial