Introduction: Patients with septic shock receive vasopressors under the assumption that correcting hypotension improves perfusion, organ function and survival. However, the association between pharmacologically enhanced blood pressure and tissue perfusion remains unclear. Vasopressor use in septic shock is influenced by guidelines that recommend aiming for a mean arterial blood pressure of 65 mmHg or more (grade 1C).

Objectives: We undertook a systematic review of clinical studies evaluating different blood pressure (BP) targets for the titration of vasopressors in septic shock. Our goal was to evaluate whether higher BP targets for vasopressor titration modified clinical outcomes in patients with septic shock when compared to lower BP targets.

Methods: We searched EMBASE, MEDLINE and CENTRAL from inception to November 2013 for observational studies and randomized controlled trials (RCTs) in humans with septic shock comparing titration of vasopressors to different target BP levels or ranges. The included studies had to report mortality, myocardial infarction, arrhythmias, need for renal replacement therapy or surrogate outcomes evaluating macro or microcirculation. Two reviewers independently assessed titles, abstracts and papers for eligibility, and abstracted data onto pretested forms. We pooled results across studies of similar design when a given outcome was reported across a minimum of 5 studies. We used the GRADE approach to summarize the quality of evidence for each outcome.

Results: We identified 4416 citations and assessed 67 full text articles for eligibility. Agreement between reviewers for relevance was moderate \( k = 0.67 \) and for eligibility, excellent \( k = 1.0 \). Two articles were identified through the grey literature. Two RCTs and nine before-after studies were included. Only one RCT comparing mean arterial blood pressure targets of 65-70 mmHg versus 80-85 mmHg assessed mortality, which was similar between groups (N = 776; hazard ratio
1.07; 95% CI 0.84, 1.38; p=0.57). However, patients in the high BP target group had a higher risk of atrial fibrillation and a lower risk of renal replacement therapy. The remaining studies evaluated short-term surrogate endpoints. When meta-analyzed, the cardiac index and heart rate in the before-after studies were significantly higher with a high BP target [7 studies, N=104; mean difference (MD) in cardiac index 0.76 L/min/m²; 95% CI 0.28, 1.24; heterogeneity X²=22.75, p

**Conclusion:** Despite one low risk of bias study evaluating clinical outcomes in septic shock patients with higher versus lower BP targets, it remains uncertain whether 65 mmHg is the optimal target. Significant harm or benefit could be associated with vasopressor titration to this target.

**References:** N/A