Introduction:
Septic shock can result in catecholamine hyposensitivity, leading to hemodynamic instability and death. Experimental data suggest that central alpha2-agonists like dexmedetomidine (DEX) increase vasopressor responsiveness and reduce catecholamine requirements in septic shock [1]. However, because it can cause hypotension and bradycardia, clinicians may be reluctant to use DEX in such patients.

Methods:
In this cohort study of the Sedation Practices in Intensive Care Evaluation (SPICE III) trial, an international randomized trial comparing sedation with DEX to usual care, we studied critically ill patients with septic shock admitted to the Austin Hospital, Melbourne, Australia, and the University Hospital of Bern, Switzerland. The primary outcome was mean noradrenaline requirements in the first 48 hours.

Results:
Between November 2013 and February 2018, 417 patients were recruited into the SPICE III trial at both sites. Eighty-three patients with septic shock were included in this sub-study, of whom 44 (53%) received DEX and 39 (47%) usual care. Mean noradrenaline dose during the first 48 hours was 0.03 [0.01, 0.07] µg/kg/min in the DEX group and 0.05 [0.01, 0.15] µg/kg/min in the usual care group (p=0.08). Over the first 48 hours, patients in the DEX group had higher mean arterial pressures (MAP) (Figure 1) and lower vasopressor requirements to maintain the target MAP (expressed by the noradrenaline equivalents to MAP ratio: NEq/MAP) compared to the usual care group (ratio of adjusted difference in geometric means 1.4 [1.1, 1.9], p=0.02).

Conclusion:
In critically ill patients with septic shock, sedation with DEX does not increase noradrenaline requirements in the first 48 hours as compared to usual care. In contrast, DEX appears to be associated with lower vasopressor requirements to maintain the target MAP.

References:
Figure 1: Mean arterial pressure in the first 48 hours after randomization

Values are presented as means, with error bars representing standard errors (P-Value=0.06, RM-ANOVA)