Introduction:
Vitamin C, an enzyme cofactor and antioxidant, could hasten the resolution of inflammation, which affects most intensive care unit (ICU) patients. While many observational studies have demonstrated that critical illness is associated with low levels of vitamin C, randomized controlled trials (RCTs) of high-dose vitamin C, alone or in combination with other antioxidants, yielded contradicting results. The purpose of this systematic review and meta-analysis is to evaluate the clinical effects of vitamin C when administered to various populations of ICU patients.

Methods:
Eligible trials: RCTs comparing vitamin C, by enteral or parenteral routes, to placebo in ICU patients. Data Collection and Analysis: We searched MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials. After assessing eligibility, data was abstracted in duplicate by two independent reviewers. Overall mortality was the primary outcome; secondary outcomes were infections, ICU length of stay (LOS), hospital LOS, and ventilator days. Pre-specified subgroup analyses were conducted to identify more beneficial treatment effects.

Results:
Pooling 9 RCTs (n=1322) reporting mortality, vitamin C was not associated with a lower risk of mortality (risk ratio [RR]: 0.84, 95% confidence interval [CI]: 0.48-1.37, P=0.44, I^2=59%). In a subgroup analysis, trials of lower quality (n= 5) were associated with a reduction in mortality (RR 0.50, 95% CI 0.32, 0.77, P= 0.002), whereas high quality trials (n= 4) were not. No statistical difference existed between subgroups (P= 0.22). In addition, no effect was found on infections, ICU or hospital length of stay, and ventilator days.

Conclusion:
Current evidence does not support the hypothesis that vitamin C supplementation improves clinical outcomes of ICU patients.