Introduction:
It is unknown whether the established association of hyponatremia with mortality is causal and whether correction of mild hyponatremia would improve survival. Our objective was to assess the independent association of change in serum sodium in the first 48 hours after ICU admission with hospital mortality.

Methods:
Multicenter cohort study in ten Dutch ICUs between January 2011 and April 2017. Inclusion criteria: patients with at least one serum sodium measurement within 24 hours of ICU-admission \([Na_1]\) and at least one serum sodium measurement 24-48 hours after ICU admission \([Na_{24-48h}]\). A Cox proportional hazard model adjusted for age, gender, and APACHE-IV score was used to assess the association between \(\Delta 48h-[Na]\) (mean-[\(Na_{24-48h}\)]-[\(Na_1\)]) and hospital mortality.

Results:
In total, 36,660 patients were included for analysis. Patients with severe hyponatremia (<125 mmol/L) and hypernatremia (>145 mmol/L) at the time of ICU admission had a higher risk of mortality. For mild hyponatremia, normonatremia, and hypernatremia at ICU admission, a \(\Delta 48h-[Na]\) >5 mmol/L was associated with larger hazards of mortality (Figure 1).

Conclusion:
An increase in serum sodium in the first 48 hours of ICU admission is independently associated with a higher mortality in patients admitted with mild hyponatremia, normonatremia, and hypernatremia. Based on our findings, it is possible that mild hyponatremia may be a protective mechanism in critical illness, which questions common practice of routinely correcting serum sodium when it is too low.
Figure 1. Association between in-hospital mortality and $\Delta_{48\text{h}}[\text{Na}]$ according to first serum sodium measurement at ICU admission.