Introduction:
While obesity confers an increased risk of death in the general population, numerous studies have reported an association between obesity and improved survival among critically ill patients. This contrary finding has been referred to as the obesity paradox. This retrospective study uses two causal inference approaches to address whether the survival of non-obese critically ill patients would have been improved if they had been obese.

Methods:
The study cohort comprises 6,557 adult critically ill patients hospitalized at the Intensive Care Unit of the Ghent University Hospital between 2015 and 2017. Obesity is defined as a body mass index of $\geq 30$ kg/m$^2$. Two causal inference approaches are used to estimate the average treatment effect in the untreated (ATU): a naive approach that uses traditional regression adjustment for confounding and that assumes missingness completely at random, and a robust approach that uses super learning within the targeted maximum likelihood estimation framework and that uses multivariate imputation of missing values under the assumption of missingness at random.

Results:
Obesity is present in 18.9% of patients. The in-hospital mortality is 14.6% in non-obese patients and 13.5% in obese patients. The marginal associational risk difference for in-hospital mortality between obese and non-obese patients is $-1.06\%$ (95% confidence interval (CI) $-3.23\%$ to $1.11\%$, $P=0.337$). The naive approach results in an ATU of $-2.48\%$ (95% CI $-4.80\%$ to $-0.15\%$, $P=0.037$), whereas the robust approach yields an ATU of $-0.59\%$ (95% CI $-2.77\%$ to $1.60\%$, $P=0.599$).

Conclusion:
A robust causal inference approach that may handle confounding bias due to model misspecification and selection bias due to missing data mitigates the obesity paradox, whereas a naive approach results in even more paradoxical findings. The robust approach does not provide evidence that the survival of non-obese critically ill patients would have been improved if they had been obese.