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Title: Antioxidants as therapeutics in the intensive care unit:  
have we ticked the redox boxes?

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## The equivocal effectiveness of antioxidants as therapeutics in the ICU

### Factors that contributed to the discrepancy in the literature

- (1) The largely unspecified role of reactive species in disease onset and progression
- (2) Our fragmentary understanding on the interplay between inflammation and oxidative stress
- (3) The complex spatiotemporal specificity of in vivo redox biology
- (4) The pleiotropic effects of antioxidants
- (5) The divergent effects of antioxidants according to the temporal administration pattern

### Novel approaches with promising pre-clinical results

- (1) The selective neutralization of reactive species in key organelles after they are formed (e.g., in mitochondria)
- (2) The targeted complete inhibition of dominant reactive species sources (e.g., NADPH oxidases).

### An alternative approach

- (1) The reductive potential of NADPH as a key pharmacological target

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