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# Faulty risk-of-bias assessment in a meta-analysis of hydroxyethyl starch for nonseptic ICU patients

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See related Research by He et al., http://www.ccforum.com/content/19/1/92

Evaluating 6 % hydroxyethyl starch (HES) of different molecular weight and substitution versus other fluids for nonseptic patients, He et al. [1] did not confirm the increased mortality, renal replacement therapy (RRT), bleeding and red blood cell transfusions seen in sepsis. A favourable safety profile for 6 % HES solutions was suggested.

He et al. stated that Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed, yet the meta-analysis lacked tests of interaction to compare different HES solutions and pre-specified subgroup analyses. The discussed limitations of the meta-analysis included study quality, heterogeneity, and problematic use [2] of gelatin as a control fluid. The Cochrane Collaboration Risk-of-Bias Tool was cited for guidance in the assessment of study quality, where any use of scales for risk of bias is explicitly discouraged because summary scores have been shown to be unreliable. He et al. calculated summary scores using a nonvalidated modified Jadad scale [3] where the highest possible score is 8, but the highest possible summary score for He et al. was only 7; reasons for this difference are obscure. Information on how assessment of risk of bias was actually performed is missing. For selective outcome reporting, the study by James et al. was wrongly judged as 'low risk' although 'high risk' had been identified previously [4, 5].

The key message from He et al. that 6 % HES does not seem to increase mortality or RRT incidence in nonseptic ICU patients is speculative because assessment of the study quality is insufficient. HES should be considered unsafe in all ICU patients until proven contrary in high-quality studies.

## Authors' response

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We thank Dr Bayer and Dr Reinhart for their comments, which we would like to nuance.

Recently, Myburgh et al. [6] reported that there was no significant difference in 90-day mortality between patients resuscitated with 6 % HES or saline. Another international multicentre large-sample randomised controlled trial (RCT) also reported the use of colloids (including HES, gelatin, dextran and albumin) versus any crystalloids for volume expansion therapy to decrease 90-day mortality [7]. In addition, two meta-analyses also showed that HES did not increase mortality or renal injury in subgroup analyses of nonseptic patients [8, 9]. Our meta-analysis also obtained similar results.

We had pre-specified subgroup analyses by different molecular weight of 6 % HES, risk of bias assessment and different kinds of fluids, all of which were found with no significant difference in mortality. We also made a brief analysis about the limitations of the meta-analysis. The Cochrane Collaboration Risk-of-Bias Tool and the modified Jadad scale were both always used for assessing the risk of bias [3, 8]. We apologise for the clerical error regarding the highest possible score in the modified Jadad scale and the inappropriate judgement for selective outcome reporting of the study by James et al.

Owing to the limitation of the current RCTs, our conclusion did not suggest using HES for these patients, and advised further RCTs of high quality for further study.

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**Abbreviations**
HES: Hydroxyethyl starch; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses; RCT: Randomised controlled trial; RRT: Renal replacement therapy.

**Competing interests**
OB received speaker's fees from CSL Behring, Germany. KR received an unrestricted research grant to conduct the VISEP trial and consultancy fees from B Braun Melsungen. The remaining authors declare that they have no competing interests.

**Authors' contributions**
KR and OB drafted the manuscript. Both authors read and approved the final manuscript.

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