Bhangu, A. Nepogodiev, D., Doughty, H., & Bowley, D. (2013) Meta-analysis of plasma to red blood cell ratios and mortality in massive blood transfusions for trauma. Injury. 44. 1693-1699. http://dx.doi.org/10.1016/j.injury.2012.07.193

Is the Study Valid?	
Did the review explicitly address a sensible clinical question?	Yes. The authors sought to "determine whether high plasma:RBC ratios during massive transfusion for trauma decrease mortality."
Were the primary studies of high methodological quality?	No. There were no RCTs available for inclusion in the meta-analysis. The 6 studies analyzed were all retrospective reviews and therefore prone to reporting and selection bias. All the studies were also prone to survival bias with only 1 of the trials formally attempting to adjust for survival bias (Maegele et al). 3 of the 6 studies excluded early deaths to include death in the ED, within 30 min of arrival, and death prior to ICU admission.
Was the search for relevant studies detailed and exhaustive?	It was fairly exhaustive. The authors searched PubMed, Cochrane Library, and Current Controlled Trials Register. They scanned the references of papers found in the search strategy and used the related studies function to identify other possible articles. Manual searching of review articles and the identified papers was also performed. The authors do not mention the inclusion of other possible sources of papers (EMBASE, abstracts from conference proceedings, etc.).
Was the selection and assessment of studies and data collection reproducible?	Yes. Inclusion criteria were clear: (i) design was randomised controlled trial (RCT), prospective observational or retrospective cohort study; (ii) included patients requiring massive blood transfusions (pre-defined as >10 units in 24 h, >6 units in 12 h or >5 units in 4 h); (iii) provided mortality data for at least two distinct patient groups based on plasma:RBC ratios transfused; (iv) comparisons were between contemporane- ous groups rather than against historical controls; (v) provided evidence that there were no significant differences in Injury Severity Score between ratio groups; (v) where there was overlap in patient cohorts between two studies, the study that contained the more recent and larger cohort was included. Exclusion criteria were clear as well: (i) case reports, letters, reviews or comments; (ii) studies that did not provide extractable mortality data for individual ratio groups; (iii) studies where ISS was different between ratio groups or where inadequate data for ISS comparison was provided; (iv) studies comparing high ratio groups to historical low ratio cohorts Data extraction from the selected articles was performed independently and then agreed upon by consensus

SYSTEMATIC REVIEW / META-ANALYSIS CRITCAL APPRAISAL SHEET

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Is the Study Valid?	
Were the results similar from study to study?	There were differences in the results from study to study. Of the 6 included trials, 4 showed benefit and 2 showed no benefit of mortality when a cut off of plasma:RBC ratios greater than 1:2 was used. Confidence intervals for all but 2 of the studies however did overlap. Tests for heterogeneity reveal that significant differences were present for all but 2 of the included articles especially when looking at the outcome of 30 day/in-hospital mortality.
What are the Results?	
What are the overall results of the review and their precision?	*For 24 hr mortality:* • For plasma:RBC ratio >1:1.5, OR = 0.34 (0.23-0.50) with low heterogeneity (2 studies) *For 30 day/in-hospital mortality:* • For plasma:RBC ratio >1:1.1, OR = 0.50 (0.37-0.68) with low heterogeneity (2 studies) • For plasma:RBC ratio of 1:2, OR = 0.49 (0.31-0.80) with **substantial heterogeneity** (4 studies) • For plasma:RBC ratio >1:2, OR = 0.56 (0.40-0.78 with **substantial heterogeneity** (6 studies) • For plasma:RBC ratio 1:2.5-1:4, OR = 0.41 (0.16-1.00) with **substantial heterogeneity** (3 studies)
How Do I Apply the Results to My Patient?	
Were all patient-important outcomes considered?	They included the patient important outcome of mortality both early (<24 hr, in-hospital, and 30 day). They wanted to look at adverse outcomes but did not find enough data in the published literature to evaluate for rates of transfusion associated lung injury, sepsis, multi-system organ failure.
Are any postulated subgroup effects credible?	There were no postulated subgroup effects
What is the overall quality of the evidence?	The overall quality of the evidence is low. In this particular meta-analysis there are no prospective studies. All studies have some risk of significant bias. There was significant heterogeneity in the results which substantially lowers the confidence in the point estimate of effect especially for 30 day and in-hospital mortality. Confidence in the estimation of effect for early (<24 hr) mortality is lowered due to the presence of a small number of articles included in the meta-analysis (2 studies).

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How Do I Apply the Results to My Patient?	
Are the benefits worth the costs and potential risks?	This particular study does not report information as to adverse events associated with the administration of higher volumes of plasma in the resuscitation of bleeding trauma patients. There is a lack of high quality evidence to support the use of high ratios of plasma:RBC however there is signal of benefit on early mortality (<24 hr) seen in 2 separate studies that, though they were both retrospective in nature, had low heterogeneity. It would be reasonable to conclude that the transfusion of plasma:RBC in a ratio >1:1.5 may provide some mortality benefit.