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## UNCERTAINTY IN TRANSFUSION PRACTICE FOR ACUTE UPPER GASTROINTESTINAL BLEEDING (AUGIB): IMPLICATIONS FOR CLINICAL TRIAL DESIGN

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**Introduction** Transfusion of red blood cells (RBCs) is a cornerstone for managing AUGIB. There has been a paradigm shift over the last decade in critical care and surgery with several studies associating RBC transfusion with adverse patient outcomes. Most relevant to decision making are recent data suggesting an association between early RBC transfusion in AUGIB and the risk of re-bleeding.

**Methods** In preparation for a proposed UK multi-centre, cluster randomised trial of restrictive versus liberal blood transfusion strategies in patients presenting with AUGIB we sought to determine: (1) the key area of clinical uncertainty in RBC transfusion practice for AUGIB; (2) the proportion of admissions likely to be eligible for trial entry; (3) estimates of the intra-cluster correlation co-efficient to inform sample size calculations for a cluster randomised phase III trial. Data was analysed from 6,750 admissions with AUGIB from the 2007 UK national audit of AUGIB and applied to potential recruiting centres for the proposed trial.

**Results** The key area of clinical uncertainty whether to transfuse patients presenting with a haemoglobin (Hb) concentration between 8.1 and 10 g/dl; in this range 51% (604/1190) of patients received transfusion and 49% (588/1190) did not and a similar degree of uncertainty persisted when patients were stratified by the absence/presence of haemodynamic shock. The Hb range 8.1-10 g/dl, together with other eligibility criteria, was used to estimate recruitment for the proposed trial. Centres meeting cluster eligibility criteria have an average 41 admissions with AUGIB/month. Under a range of clinical scenarios anywhere between 26.4% to 44.8% of new admissions with AUGIB will meet trial eligibility criteria. Intra-cluster correlation co-efficient (ICC) range between 0.007-0.015; assuming an ICC of 0.01 and 30 centres for a phase III trial, 44 patients per centre would be required to detect a 5% reduction in re-bleeding from 15% to 10%, across 30 centres with 90% power and 5% significance by use of a restrictive transfusion practice.

**Conclusion** Cluster randomised trials are useful designs for pragmatic trials measuring the effectiveness of an intervention in routine clinical practice. They have unique challenges in design, conduct and analysis. Detailed observational data from the UK national audit of AUGIB has enabled key methodological components to be addressed for a cluster-randomised trial of restrictive versus liberal transfusion practice in AUGIB.

**Competing interests** None.

**Keywords** gastrointestinal bleeding, gastrointestinal haemorrhage, randomised controlled trial.