**Appendix Table 4. Areas of Future Research**

### Pre-endoscopy
- Timing of initial endoscopy in relation to a clinical scale of low vs. high risk (Blatchford, Rockall) and optimal predictive models
- Role of early discharge of very low risk patients (very low Blatchford) without endoscopy vs. early endoscopy or overnight observation until endoscopy
- Optimal INR correction and endoscopic treatment of patients with UGIB on an anticoagulant, and in the setting of thrombocytopenia
- The optimal minimal platelet level to be targeted in patients with acute UGIB
- Role of prokinetics in patients with hematemesis or blood in the naso-gastric aspirate

### Endoscopic therapy
- Comparative roles of newer endoscopic modalities for hemostasis
- Role of second-look endoscopy in the era of profound acid suppression
- Role of endoscopic therapy vs. acid suppression alone in adherent clots
- Role of percutaneous embolization and surgery vs. repeat endoscopy after failure of endoscopic therapy
- Real-life data to confirm the efficacy results and ensure adequate dissemination of guidelines

### PPI and other pharmacological therapy
- Optimal route of administration, dose, and duration of PPI following successful endoscopic hemostasis (direct comparison of oral versus intravenous PPI)
- Role of early switch from intravenous to oral PPI, and optimal dose and duration of PPI therapy following discharge
- Clarification of potential PPI-related complications and drug interactions
- Role of octreotide as an alternative to intravenous PPIs both pre- and post-endoscopy

### Classification of stigmata
- Revision of the Forrest 1B (oozing bleeding) classification and clarification of the risk of rebleeding of adherent clots in clinically high and low risk patients
- Standardization and validation of an objective measure to classify stigmata
- Improved training of endoscopists (classification of stigmata and effective hemostasis)

### ASA and NSAID related issues
- Optimal timing of reinstatement of ASA therapy in patients with acute UGIB
- Impact of clopidogrel on endoscopic hemostasis and risk of rebleeding
- Gastrointestinal and cardiovascular risk:benefit ratio for PPI + NSAID versus PPI + COX-2 inhibitor in patients with a history of UGIB
- Role of PPI in patients with UGIB who require continued clopidogrel therapy
- Risk of combination ASA + clopidogrel + PPI in patients with a previous ulcer bleed
- Clinical importance of clopidogrel–PPI interaction

### Economics
- Additional cost-effectiveness analyses to better characterize diagnostic and therapeutic strategies

ASA=acetylsalicylic acid, COX-2=cyclooxygenase-2, INR=international normalized ratio, PPI=proton pump inhibitor, UGIB=upper gastrointestinal bleed