SUP-ICU trial

Title	Stress Ulcer Prophylaxis in the Intensive Care Unit
Short title	SUP-ICU
Objectives	To assess benefits and harms of stress ulcer prophylaxis (SUP) with proton pump inhibitors (PPI) in adult critically ill patients in the intensive care unit (ICU)
Population	Adult critically ill patients in the ICU with one or more risk factors for GI bleeding
Interventions	Intravenous pantoprazole 40 mg (10 ml) once daily until death or discharge from the ICU
Comparator	Intravenous saline (10 ml) once daily until death or discharge from the ICU
Outcomes	***Primary*** All cause 90-day mortality (post-randomization) ***Secondary*** 1. Proportion of patients with one or more of the following adverse events: clinically important gastrointestinal (GI) bleeding, pneumonia, *clostridium difficile* infection (CDI), or acute myocardial ischemia in the ICU 2. Proportion of patients with clinically significant GI bleeding in the ICU 3. Proportion of patients with one or more infectious adverse events (pneumonia or CDI) in the ICU 4. 1-year "landmark" mortality post-randomization 5. Days alive without the use of mechanical ventilation, renal replacement therapy or circulatory support in the 90-day period 6. Number of serious adverse reactions 7. A health economic analysis will be performed. The analytic details will be based on the result of the trial and specified (cost-benefit vs cost-minimisation analyses) The specific elements of the composite outcomes will be reported in the supplementary material of the primary publication.
Eligibility	***Inclusion criteria*** 1. Acute admission to the ICU 2. Age ≥ 18 years 3. One or more of the following risk factors for GI bleeding: • Shock (continuous infusion with vasopressors or inotropes, systolic blood pressure < 90 mmHg, mean arterial blood pressure < 70 mmHg or lactate > 4 mmol/l) • Acute or chronic intermittent or continuous renal replacement therapy • Invasive mechanically ventilation which is expected to last > 24 hours. • Coagulopathy (platelets < 50 x 109/l or international normalized ratio (INR) > 1.5 or prothrombin time (PT) > 20 seconds) documented within the last 24 hours • Ongoing treatment with anticoagulant drugs (prophylaxis doses excluded) • History of coagulopathy (platelets < 50 x 109/l or INR > 1.5 or PT > 20 seconds within 6 months prior to hospital admission • History of chronic liver disease (portal hypertension, cirrhosis proven by biopsy, computed tomography (CT) scan or ultrasound, history of variceal bleeding or hepatic encephalopathy in the past medical history) ***Exclusion criteria*** 1. Contraindications to PPI (including treatment with atazanavir (HIV medication)) 2. Ongoing treatment with PPI and/or histamine-2-receptor antagonist on a daily basis 3. GI bleeding of any origin during current hospital admission 4. Diagnosed with peptic ulcer during current hospital admission 5. Organ transplant during current hospital admission 6. Withdrawal from active therapy or brain death 7. Fertile woman with positive urine human chorionic gonadotropin (hCG) or plasma-hCG 8. Consent according to national regulations not obtainable
Sample size	2 x 1675 (20% relative risk reduction or increase (5% absolute risk reduction or increase) in the primary outcome measure, assuming a baseline 90-day mortality of 25% (two-sided α=0.05 and β=0.1)
Study duration	A maximum of 90 days post-randomizations. 90 days and 1 year follow-up post-randomization. Estimated recruitment period is 2 years commencing June 2015