

SUPPLEMENTARY FILE 2: ELIGIBILITY CRITERIA AND ENROLMENT PERIODS

This is a supplementary file to the paper: **“THE SIMPLIFIED MORTALITY SCORE FOR THE INTENSIVE CARE UNIT (SMS-ICU): Protocol for the development and validation of a bedside clinical prediction rule“**.

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This supplement contains additional details regarding eligibility criteria and enrolment periods in the studies/trials used in the Simplified Mortality Score for the Intensive Care Unit (SMS-ICU) project. For further details, including treatment protocols, please refer to the original publications or protocols.

Scandinavian Starch for Severe Sepsis/Septic Shock (6S) trial

Screening and randomisation took place between December 23, 2009 and November 15, 2011. Eligibility criteria adapted from ClinicalTrials.gov registration (NCT00962156) and the primary 6S publication.[1]

Inclusion criteria:

All adult patients (18 years and older) who:

- Undergo resuscitation in the intensive care unit (ICU) AND
- Fulfilment within the previous 24 hours of the criteria for severe sepsis (Society of Critical Care Medicine/American College of Chest Physicians definition) AND
- Consent is obtainable either from the patient or by proxy (physician and/or next of kin)

Exclusion criteria:

- Age < 18 years old
- Previously randomised in the 6S trial
- Allergy towards hydroxyethyl starch or malic acid

- Treatment with > 1000 ml of any synthetic colloid within the last 24 hours prior to randomisation
- Any form of renal replacement therapy (RRT)
- Acute burn injury > 10% body surface area
- Severe hyperkalaemia, p-K > 6 mM
- Liver or kidney transplantation during current hospital admission
- Intracranial bleeding within current hospitalisation
- Enrolment into another ICU trial of drugs with potential action on circulation, renal function or coagulation

Transfusion Requirements In Septic Shock (TRISS) trial

Screening and randomisation took place between December 3, 2011 and December 26, 2013. Eligibility criteria adapted from ClinicalTrials.gov registration (NCT01485315) and the primary TRISS publication.[2]

Inclusion criteria:

- Patient in the ICU AND
- Fulfil the criteria for septic shock AND
- Have haemoglobin of 9.0 g/dl (5.6 mM) or less AND
- Consent obtainable from patient or proxy or national law allows delayed consent

Exclusion criteria:

- Documented wish against transfusion OR
- Previous serious adverse reaction with blood product OR
- Acute coronary syndrome OR
- Life-threatening bleeding OR
- Red blood cell transfusion during current ICU admission OR
- Withdrawal from active therapy or brain death OR
- Lack of informed consent (depending on national law) OR
- Acute burn injury regardless of degree and burn surface area

Conservative vs. Liberal Approach to fluid therapy of Septic Shock in Intensive Care (CLASSIC) trial

Screening and randomisation took place between September 2014 and August 2015. Eligibility criteria adapted from ClinicalTrials.gov registration (NCT02079402) and the CLASSIC publication.[3]

Inclusion criteria:

- Adult intensive care patients (age \geq 18 years) with sepsis defined as 2 of 4 systemic inflammatory response syndrome (SIRS) criteria fulfilled within 24 hours and suspected or confirmed site of infection or positive blood culture.
- Suspected or confirmed circulatory impairment (hypotension/hypoperfusion/hypovolemia) for no more than 12 hours including the hours preceding ICU admission.
- At least 30 ml/kg ideal body weight fluid (colloids, crystalloids or blood products) given in the last 6 hours.
- Shock defined as ongoing infusion of norepinephrine (any dose) to maintain blood pressure.

Exclusion criteria:

- Use of any form of RRT
- RRT deemed imminent by the ICU doctor, i.e. RRT will be initiated within 6 hours.
- Severe hyperkalemia (p-K $>$ 6 mM).
- Plasma creatinine $>$ 350 μ mol/l.
- Invasively ventilated with fraction of inspired oxygen (FiO₂) $>$ 0.80 and positive end-expiratory pressure (PEEP) $>$ 10 cm H₂O.
- Life-threatening bleeding.
- Kidney or liver transplant during current admission.
- Burns $>$ 10% body surface area
- Previously enrolled in the CLASSIC trial and has finished the 90-day observation period.
- Patients for whom it has been decided not to give full life support including mechanical ventilation and RRT.
- Consent not obtainable.

Stress Ulcer Prophylaxis in the Intensive Care Unit (SUP-ICU) inception cohort study

Screening and inclusion took place between December 1, 2013 and April 30, 2014.

Eligibility criteria adapted from the SUP-ICU inception cohort publication.[4]

Inclusion criteria:

- Adult (age \geq 18 years) critically ill patients admitted acutely to one of the study ICUs (n=97).

Exclusion criteria:

- Age < 18 years
- Observed upper gastrointestinal (GI) bleeding and/or treatment for upper GI bleeding during current hospital admission.
- Planned ICU admission (e.g. after elective surgery).
- Previous ICU admission during current hospital admission before the 7-day study period.

Agents Intervening against Delirium in Intensive Care Unit (AID-ICU) inception cohort study

Screening and inclusion took place between March 1, 2016 and June 30, 2016.

Eligibility criteria adapted from the AID-ICU inception cohort protocol.[5]

Inclusion criteria:

- Adult (age \geq 18 years) critically ill patients admitted acutely to one of the participating ICUs during the 14-day inception period.

Exclusion criteria:

- Pre-diagnosed mental illness of schizophrenia and/or psychosis and/or major depression (ICD 10; F20-29 F30, F31, F32, F33)
- Terminal status (i.e., expected to survive < 24 hr. and/or withdrawal of life-support)
- Pre-diagnosed neurodegenerative disorders Dementia and Parkinson (ICD 10; F02-04)

- Mental illness recurring institutionalization or acquired or congenital mental retardation
- Patients with congenital or acquired brain damage, i.e.; stroke in the past 2 weeks, transient cerebral ischemic in the past 2 weeks, subarachnoid haemorrhage, cerebral cancer, meningitis, encephalopathies, ongoing seizures and suspected anoxic brain injury or traumatic brain injury
- Patients admitted with hepatic coma, drug overdose or suicide attempt (within the past 6 months necessitating hospitalization)
- Blind and/or deaf

SUP-ICU trial

Screening and randomisation of the first patient took on January 4, 2016, and enrolment in the trial is expected to conclude at the end of 2017. Eligibility criteria adapted from the ClinicalTrials.gov registration (NCT02467621) and the published protocol.[6]

Inclusion criteria:

- Acute admission to the ICU
- Age \geq 18 years
- One or more of the following risk factors:
 - o Shock (continuous infusion with vasopressors or inotropes, systolic blood pressure $<$ 90 mmHg, mean arterial blood pressure $<$ 70 mmHg or lactate $>$ 4 mmol/l)
 - o Acute or chronic intermittent or continuous RRT
 - o Invasive mechanical ventilation which is expected to last $>$ 24 hours
 - o Coagulopathy (platelets $<$ $50 \times 10^9/l$ or international normalized ratio (INR) $>$ 1.5 or prothrombin time (PT) $>$ 20 seconds) documented within the last 24 hours
 - o Ongoing treatment with anticoagulant drugs (prophylaxis doses excluded)
 - o History of coagulopathy (platelets $<$ $50 \times 10^9/l$ or INR $>$ 1.5 or PT $>$ 20 seconds) within 6 months prior to hospital admission
 - o History of chronic liver disease (portal hypertension, cirrhosis proven by biopsy, computed tomography scan or ultrasound, history of variceal

bleeding or hepatic encephalopathy in the past medical history)

Exclusion criteria:

- Contraindications to proton pump inhibitors (PPI)
- Ongoing treatment with PPI and/or histamine-2-receptor antagonists on a daily basis
- GI bleeding of any origin during current hospital admission
- Diagnosed with peptic ulcer during current hospital admission
- Organ transplant during current hospital admission
- Withdrawal from active therapy or brain death
- Fertile woman with positive urine- or plasma human chorionic gonadotropin
- Consent according to national regulations not obtainable

References

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- [3] Hjortrup PB, Haase N, Bundgaard H, et al. Restricting volumes of resuscitation fluid in adults with septic shock after initial management: the CLASSIC randomised, parallel-group, multicentre feasibility trial. *Intensive Care Med* 2016;42: 1695-1705. doi:10.1007/s00134-016-4500-7
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