Research questions for the update of the PBM Guidelines (Modules 2-6)

| Theme # | Theme | Active question | Population  *Subgroups* | Intervention(s) | Critical outcome(s) |
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| **1** | **Effect of a PBM program** | **U1-GQ01** | All patients   * *Perioperative* * *Medical* * *Critical care* * *Obstetrics and maternity* * *Neonatal and paediatrics* | PBM program | * Mortality * Transfusion |
| **2** | **Effect of RBC transfusion** | **U1-GQ02** | All adult patients   * *Perioperative* * *Medical* * *Critical care* | RBC transfusion | * Mortality |
|  |  | **U1-Q25** | Neonatal and paediatric patients | RBC (allogeneic) transfusion | * Mortality * Composite of mortality and severe morbidity * Neurodevelopmental disability * Necrotising enterocolitis |
| **3** | **Restrictive vs. liberal transfusion strategies** | **U1-GQ03** | All patients   * *Perioperative* * *Medical* * *Critical care* * *Obstetrics and maternity* * *Neonatal and paediatrics* | Restrictive vs. liberal RBC transfusion | * Mortality * Transfusion * Neurodevelopmental disability *(neonatal only)* * Necrotising enterocolitis *(neonatal only)* |
| **4** | **Optimal Hb threshold for transfusion** | **U1-Q20** | Chronically transfused patients   * *Paediatrics* * *Myelodysplasia* | RBC transfusion (at different Hb thresholds) | * Mortality/survival * Functional/performance status |
| **5** | **Effect of blood component therapy** | **U1-GQ06** | Patients receiving anti-platelet medication   * *Perioperative* * *Medical* * *Critical care* | Platelet transfusion | * Mortality * Blood component utilisation * Bleeding into critical sites/organs * Major bleeding |
|  |  | **U1-Q22** | Patients with critical bleeding   * *Perioperative* * *Obstetrics* * *Paediatric patients* | Cryoprecipitate  vs.  Fibrinogen concentrate | * Mortality * Blood component utilisation |
|  |  | **U1-Q26** | Neonatal and paediatric patients   * *Surgical* * *Trauma* * *Critical illness* | 1. Platelet transfusion *(preterms and newborns)*  2. Fibrinogen concentrate *(paediatric surgical and trauma patients)* | * Mortality * Major bleeding * Intraventricular haemorrhage *(neonatal only)* * Blood component utilisation |
| **6** | **Trigger for blood component therapy** | **U1-GQ04** | All patients   * *Perioperative* * *Medical* * *Critical care* * *Obstetrics and maternity* * *Neonatal and paediatrics* | Platelet transfusion | * Mortality * Bleeding in previously non-bleeding patients (including intracranial haemorrhage for neonates) * Bleeding into critical sites/organs * ischaemic/thromboembolic events * Blood component utilisation |
|  |  | **U1-GQ05** | Patients with acquired abnormalities of haemostasis   * *Perioperative* * *Medical* * *Critical care* * *Obstetrics and maternity* * *Neonatal and paediatrics* | 1. Plasma transfusion or prothrombinex (at an INR threshold)  2. Cryoprecipitate or fibrinogen concentrate (at a specific fibrinogen level)  3. Platelet transfusion (at a specific platelet count) (included in GQ04)9  4. Blood component therapy based on viscoelastic testing | * Mortality * Major bleeding * Intracranial haemorrhage *(neonatal only)* * Ischaemic or thromboembolic events * Blood component utilisation |
| **7** | **Effect of cessation of medications that affect haemostasis** | **U1-Q17** | 1. Surgical patients  2. Patients undergoing invasive procedures | Anti-coagulants and anti-platelet therapy, including aspirin, clopidogrel, direct-acting anti-coagulants, warfarin | * Mortality * Transfusion * Procedure-related bleeding * Reoperation for bleeding * Ischaemic or thromboembolic events |
| **8** | **Effect of non-transfusion interventions** | **U1-Q16** | Surgical patients   * *Preoperative* * *Intraoperative* * *Postoperative* | 1. Iron therapy (oral and/or parenteral) | * Mortality * RBC transfusion |
|  |  | **U1-Q19** | Medical patients   * *Haematology oncology* * *Renal* * *Congestive heart failure* | 1. ESAs  2. Iron therapy (oral or parenteral IV or IM)  3. Combination of these | * Mortality * RBC transfusion * Ischaemic or thromboembolic events |
|  |  | **U1-Q21** | Critically ill patients | 1. Iron therapy (parenteral IV)  2. ESAs  3. Combination of these | * Mortality * RBC transfusion * Ischaemic or thromboembolic events |
|  |  | **U1-Q23** | Obstetrics and maternity patients | 1. Iron therapy (oral and/or parenteral IV) | * Mortality (maternal) * Transfusion * Measures of fetal outcome |
| **9** | **Effect of blood conservation strategies** | **U1-Q18** | Surgical patients  Patients undergoing invasive procedures (TXA only)   * *Obstetrics* | 1. Cell salvage (perioperative)  2. Deliberate induced hypotension  3. POC testing for coagulation status and Hb  4. Restrictive sampling  5. Administration of antifibrinolytics (TXA, aprotinin) and DDAVP | * Mortality * Transfusion |
|  |  | **U1-Q24** | Obstetrics and maternity patients   * *Bleeding patients (postpartum/antepartum haemorrhage, placenta problems, ectopic pregnancy, miscarriage)* | 1. Viscoelastic testing  2. Administration of antifibrinolytics (TXA only)  3. Cell salvage (intraoperative)  4. Interventional radiology (iliac balloon catheters or embolisation only) | * Mortality (maternal) * Transfusion |
|  |  | **U1-Q27** | Neonatal patients  Paediatric patients   * *Surgical (cardiac, burns, transplantation, orthopaedic)* * *Critical illness (ECMO/ECLS, trauma)* | Preterm and newborn  1. Placental transfusion  Infant/child/adolescent – surgical  1. Deliberate controlled/induced hypotension  2. Cell salvage (intraoperative)  3. Viscoelastic testing  4. Administration of antifibrinolytics (TXA, aprotinin)  Infant/child/adolescent – critical illness  1. Viscoelastic testing | Preterm and newborn   * Composite death and/or major morbidity * Transfusion * Mortality * Neurodevelopmental outcomes   Infant/child/adolescent – surgical/critical illness   * Mortality * Transfusion * Neurodevelopmental outcomes * Major bleeding * Intraventricular haemorrhage (neonatal only) |

Abbreviations: DDAVP, desmopressin; ECLS, extracorporeal life support; ECMO, extracorporeal membrane oxygenation; ESA, erythrocyte-stimulating agents; Hb, haemoglobin; IM, intramuscular; IV, intravenous; IVIg, intravenous immunoglobulin; LBW, low birth weight; NSAID, non-steroidal anti-coagulant; POC, point-of-care; RBC, red blood cell; TXA, tranexamic acid.