**SUPPLEMENTAL DIGITAL CONTENT 1. Outcome categories**

**A) Outcomes associated to or worsened by anemia:**

**> Events reflecting inadequate oxygen supply:**

Only in-hospital or 30-day events were retrieved. In studies reporting both, only the longest time-period was considered. The following events were included:

>> Myocardial infarction, arrhythmia, unstable angina;

>> Stroke or transient ischemic attack;

>> Acute kidney injury (AKI), defined as an increase in creatinine levels or the need for renal replacement therapy. Acute kidney injury has been suggested to have a multifactorial origin and may result not only from renal hypoxemia (induced by hypotension or hypovolemia), but also from other stressors, such as systemic inflammation or oxidative stress.1 We assumed that any difference in AKI rates between transfusion strategies would most likely reflect anemia-induced hypoxia, since randomization should ensure that other stressors are well balanced between groups.

>> Mesenteric or peripheral ischemia.

**> Early mortality:** in-hospital or 30-day mortality rates. In studies reporting both, only the longest time-period was considered.

**> Composite events:** combination of events reflecting inadequate oxygen supply and early mortality.

**B) Outcomes related to immunomodulatory effects of allogeneic blood:**

**> Incidence of** **infections**: defined as any type of infection. In studies reporting several infection subtypes, data were combined to obtain an overall infection rate. When studies reported just one subtype, this rate was considered as the overall infection rate.

**Note:** Outcomes such as **"pulmonary edema"** or **"acute lung injury"** were not considered, since the distinction between events caused by immunological reactions and those due to circulatory overload or heart failure was deemed difficult to draw. We assumed infection rates more representative and informative of immunomodulatory effects related to blood transfusions.

**REFERENCES**

1. Karkouti K, Wijeysundera DN, Yau TM, McCluskey SA, Chan CT, Wong PY, Crowther MA, Hozhabri S, Beattie WS. Advance targeted transfusion in anemic cardiac surgical patients for kidney protection: an unblinded randomized pilot clinical trial. *Anesthesiology.* 2012;116(3):613-621.