**Supplemental Digital Content 4. Data handling, transformation and combination**

**> Data handling:** outcomes belonging to the same dimension but reported separately. For instance, we merged "increase in creatinine" and "need for renal replacement therapy" into "acute kidney injury".

**> Data transformation:** (1) hematocrit (Hct) values were converted into hemoglobin (Hb) values using the formula "Hb [g/dL] = Hct [%]/3" as described elsewhere;1 (2) transfusion volumes expressed in milliliters were converted in erythrocyte units using the formula "300mL = 1 erythrocyte unit", as described elsewhere.2

**> Data combination:** for each study, composite outcome data were obtained by adding up the number of individual events, as performed in previous reports.2,3 For instance, composite outcome data (events reflecting inadequate oxygen supply + mortality) in the restrictive group of Murphy 2015 (328/1000) were computed by adding up myocardial infarction (1 event), arrhythmia (151 events), acute kidney injury (134 events), stroke (11 events) mesenteric ischemia (5 events) and death (26 events).

**REFERENCES**

1. Desjardins P, Turgeon AF, Tremblay MH, Lauzier F, Zarychanski R, Boutin A, Moore L, McIntyre LA, English SW, Rigamonti A, Lacroix J, Fergusson DA. Hemoglobin levels and transfusions in neurocritically ill patients: A systematic review of comparative studies. *Critical Care.* 2012;16(2).

2. Carson JL, Carless PA, Hebert PC. Transfusion thresholds and other strategies for guiding allogeneic red blood cell transfusion. *The Cochrane database of systematic reviews.* 2012;4:CD002042.

3. Rohde JM, Dimcheff DE, Blumberg N, Saint S, Langa KM, Kuhn L, Hickner A, Rogers MA. Health care-associated infection after red blood cell transfusion: a systematic review and meta-analysis. *JAMA.* 2014;311(13):1317-1326.