

Supplemental material 1: search strategies

Search date: 2020/09/25

A. Embase

- #1. 'intensive care unit'/exp OR ((intensive OR critical) NEAR/1 care OR ICU OR ITU OR (close-attention OR intensive-treatment OR intensive-therapy) NEAR/1 unit*):ab,ti,kw
- #2. 'anemia'/exp OR (anemia OR anaemia):ab,ti,kw
- #3. #1 AND #2 7432
- #4. 'clinical study'/de OR 'case control study'/de OR 'family study'/de OR 'longitudinal study'/de OR 'retrospective study'/de OR 'cohort analysis'/de OR ('prospective study'/de NOT 'randomized controlled trials'/de) OR ((cohort OR case-control OR follow-up OR observational OR epidemiologic* OR cross-sectional) NEAR/1 (study OR studies)):ab,ti,kw
- #5. #3 AND #4 1878

B. PubMed

- #1. "Intensive Care Units"[Mesh] OR "Critical Care"[Mesh] OR "intensive care"[Title/Abstract] OR "critical care"[Title/Abstract] OR ICU[Title/Abstract] OR ITU[Title/Abstract] OR "close attention unit"[Title/Abstract] OR "intensive treatment unit"[Title/Abstract] OR "intensive therapy unit"[Title/Abstract] OR "close attention units" or "intensive treatment units"[Title/Abstract] OR "intensive therapy units"[Title/Abstract]
- #2. "Anemia"[Mesh] OR Anemia[Title/Abstract] OR anaemia[Title/Abstract]
- #3. #1 AND #2 2046
- #4. "Case-control studies"[MeSH Terms] OR "Cohort studies"[MeSH Terms] OR "Case control*"[Text Word] OR "cohort study"[Text Word] OR "cohort studies"[Text Word] OR "cohort analysis"[Text Word] OR "cohort analyses"[Text Word] OR "observational study"[Text Word] OR "observational studies"[Text Word] OR retrospective[Text Word] OR "cross-sectional"[Text Word] or "cross sectional"[Text Word] OR prospective[Text Word] OR "Cross-sectional studies"[Mesh]
- #5. #3 AND #4 882

C. Web of Science

- #1. TS=((intensive or critical) near/1 care OR ICU OR ITU OR ("close attention" or "intensive treatment" or "intensive therapy") near/1 unit*)

#2. TS=(anemia or anaemia)

#3. #1 AND #2 1957

#4. TS=((clinical OR "case control" OR family OR longitudinal OR retrospective OR prospective OR cohort OR "follow up" OR "follow-up"
OR observational OR epidemiological OR "cross sectional" or "cross-sectional") near/1 (study or studies))

#5. #3 AND #4 597

Supplemental table S1: Characteristics of included papers.

Study ID	Study design	Sample size	Diagnosis	Inclusion Criteria	Age (years old)	Male/female	Outcome category	Duration of follow-up	Risk Factors	Definition of Risk Factors
Alves 2010	Case control study	84	The diagnosis at ICU admission were post-surgery, stroke, neoplasm, septic shock,	All patients older than 60 years-old admitted to the ICU from	73 (60-89)	34/50	Death	NR	Anemia measured at admission and during	Hemoglobin <13 g/dL for men and <12 g/dL for women.

				Hypovolemic shock, Respiratory failure, Cardiogenic shock and other.	January to December 2007 were included.				hospital stay	
Ameloot 2015	Cohort study	82	NR	All comatose survivors after non-traumatic cardiac arrest treated in our tertiary care hospital are prospectively enrolled.	63± 13	57/25	Good neurological outcome; Death	180 days post-cardiac arrest	Hemoglobin	An arterial blood gas with determination of hemoglobin was taken hourly during the 24 h hypothermia period. Hemoglobin values were divided in

quartiles.

da Silva 2006	Cohort study	128	Acute renal failure	All patients who presented acute renal failure during ICU stay.	49.5± 20.6	79/49	All-cause mortality	17 ± 15 days	Hemoglobi n	Continuous variable
Ergan 2016	Cohort study	106	COPD	All consecutive COPD	71(62- 76)	83/23	Hospital mortality; Noninvasiv	NR	Anemia Hemoglobi n levels	Hemoglobin levels ,12 gm/dL for

				exacerbation			e		female patients	
				patients who			ventilation		and ,13 gm/dL	
				developed			failure;		for male	
				acute			Long-term		patients	
				respiratory			survival		according to the	
				failure.					World Health	
									Organization	
									(WHO) anemia	
									definition	
Gadren	Cohort	1107	COPD	All patients	64±	544/	90 –day	90 days	Anemia	Hemoglobin
2017	study			with COPD	12.7	563	mortality;		Hemoglobi	levels<12 g/dL
				having acute			overall		n levels	at ICU
				respiratory			mortality			admission.
				failure due to						
				any cause						
				admitted to the						
				medical ICU						

Hamilton 2015	Cohort study	140	Severe burns	Patients with thermal injuries with a total body surface area burn of greater than 20% or with inhalation injury.	26 ± 6.4	130/5	Hospital days ICU days; Ventilation days; Sepsis; Acute respiratory distress syndrome; Ventilator-associated pneumonia; Renal failure; Mortality	30 days	Anemia	Hemoglobin at the time of theater evacuation < 10 g/dL.
Han	Cohort	2145	Cardiovascular	Patients were	67.5 ±	1281/	Acute	The first 15	Anemia	Hemoglobin

2015	study	disease, Sepsis, Surgical emergency, Underlying chronic kidney disease, Diabetes mellitus, Non-hematologic malignancy, Hematologic malignancy, Previously diagnosed anemia, Bleeding.	admitted to the ICU during the period of the study.	15.88	864	kidney injury; Early acute kidney injury; Late acute kidney injury; Non-recovered AKI; All-cause mortality; Length of hospital stay	days of the ICU admission.	level <10.5 g/dL		
Ittyachen 2016	Cohort study	70	COPD	COPD with supporting	NR	61/9	All-cause mortality	6 days	Anemia	hemoglobin: males <13 g %

				spirometry or a high probability of the disease (on the basis of clinical history, history of chronic exposure to respiratory irritants, smoking history, physical examination, and chest radiograph)						and females <12 g %).
Kopterides 2011	Cohort study	126	Cancer	Adult patient (>18 years old) with a pathologically	65.35± 14.42	76/50	All-cause mortality	Median (IQR): 6 (4-16) days	Anemia	Hemoglobin level < 10 g/dL

				proven cancer who required ICU admission.						
Kristof 2018	Cohort study	435	Sepsis	General surgical ICU patients with sepsis excluding cardiac surgery patients	62±15	278/ 157	Death	90 days	Anemia requiring red blood cell transfusion	NR
Kurtz 2010	Cohort study	34	Severe brain injury caused by subarachnoid hemorrhage	Severe brain injury caused by subarachnoid hemorrhage that underwent	52 (27– 84)	11/23	Brain tissue hypoxia	NR	Hemoglobi n ranges	divided into 4 group: ≤9,9.1-10,1.1-1 1, > 11g/dL

multimodality
 neuromonitorin
 g of
 intracranial
 pressure (ICP),
 cerebral micro
 dialysis, and
 PbtO2 as part
 of their clinical
 care.

Lee 2015	Cohort study	6500	Trauma	All patients admitted to the ICU setting following initial trauma evaluation and resuscitation,	PRE:4 2 years; EARL Y: 52 years; MAT	2288/4 212	Mortality	6 years	Anemia	NR
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				and had to have an ICU length of stay (LOS) ≥ 1 day	URE: 62 years;					
Lee 2016	Cohort study	362	peritonitis postoperatively	Patients who underwent emergency GI surgery for peritonitis	64.1 \pm 14.4	212/13 7	In-hospital mortality	NR	Anemia	Hemoglobin <10g/dL, both preoperative and postoperative
Lipsic 2005	Cohort study	1769	Acute myocardial infarction	Peak creatinine kinase (CK) plasma levels above 500 IU/l during the first 96 h of hospitalization	62.2 \pm 0.3	1293/ 476	All-cause mortality	30 days	Anemia	Hemoglobin ≤ 10 g/dl

Moham madi 2018	Case control study	900	ICU patients	All patients who admitted to the ICU with a length of stay greater than 48 h.	54.7± 8.2	504/ 396	Developme nt of acute kidney injury	6 months after hospital discharge	Anemia	Hemoglobin<10 g/Dl
Mora 2014	Case control study	1252	Traumatically injured	Traumatically injured subjects with a recorded pre-flight hemoglobin value were enrolled.	hemog lobin >8.0 g/dL group: 24 (21-2 9) ; hemog lobin≤ 8.0	1233/ 19	Incidence of complicatio ns Mortality Hospitalize d Return to duty Incidence of infection Incidence	30 days	Anemia	Both two criteria: hemoglobin<8 g/dL and 7 g/dL were analysed.

					g/dL		of patients			
					group:		at 30 days			
					25		receiving			
					(22-2		inpatient			
					9)		care			
Mukho	Case	1563	Sepsis	Patients (≥ 18	NR	957/60	Mortality	52 months	Hemoglobi	NR
padhya	control		(Pulmonary,	years) who		6	following		n	
y 2014	study		Others)	were admitted			hospital			
			Organ-specific	to ICU from			discharge			
			disease(Hepatic,N	January 2008						
			eurological,Renal,	to April 2010.						
			Cardiovascular,En							
			docrine,Pulmonary							
)							
			Malignancy							
			(Hematological,							
			Nonhematological)							

Others										
Oral 2016	Case control study	186	Pneumonia	Patients with pneumonia hospitalized in intensive care unit.	Total: 63.7± 20.5	104/82	Unfavorabl e outcome	30 days	Anemia (Hgb≤9 g/dl) and simultaneo us brain hypoxia (PbtO2< 20 mmHg)	NR
Okoye 2013	Cohort study	812	Traumatic brain injury	Included patients had a history of head trauma and an intracranial abnormality on initial head computed	48± 23	633/17 9	Overall mortality Hospital length of stay Intensive care unit length of	7 years	Hemoglobi n, g/dL	Three ways of grouping: ≤8g/dL and > 8g/dL (Non-anemic); ≤9g/dL and > 9g/dL (Non-anemic);

tomography.							stay	≤10g/dL and		
							Acute renal	> 10g/dL		
							failure,	(Non-anemic).		
							Acute			
							respiratory			
							distress			
							syndrome,			
							Sepsis			
							during their			
							hospital			
							stay			
Park	Cohort	51	Solid cancer	Solid cancer	65	38/13	Intensive	NR	Anemia	Anemia was
2013	study		patients with acute	patients with	(25-87		care unit			defined as a
			respiratory failure	acute)		mortality			hemoglobin
				respiratory						level less than
				failure						12g/dL.
				requiring						

invasive
mechanical
ventilation and
who had
received
ambulatory
chemotherapy
within 1 month
of ICU
admission
were included.

Powell 2016	Case control study	210	Acute kidney injury	Meet the criteria for acute kidney injury stage I within 12 hours.	70 (57– 77)	142/68	Progression from acute kidney injury I to acute kidney	NR	Hemoglobi n, g/L	Continuous variable
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injury III

Rasmus sen 2011	Cohort study	222	Chronic obstructive pulmonary disease	All patients older than 35 years admitted for the first time to our intensive care unit with acute respiratory failure and requiring invasive	NR	100/ 122	30-day mortality 90-day mortality	30 days after intensive care unit admission	Anemia	Three levels of hemoglobin were defined: anemia: hemoglobin < 7.4mmol/L (< 12.0g/dL); normal: 7.4-9.3mmol/L (12.0-15.0g/dL) ; high: >9.3
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				mechanical ventilation were identified in the database.						mmol/L (15.0g/dL).
Salim 2008	Case control study	1150	Blunt traumatic brain injury	All patients with serial hemoglobin measurements were included in the study.	40± 21	859/ 291	Hospital stay (including deaths) Hospital stay (excluding deaths) ICU stay (including deaths) Mortality Complicati	NR	Anemia	Anemia was defined as a hemoglobin level of less than 9 g/dL for 3 consecutive measurements.

							ons			
Simoes	Case	308	Cancer patients	Patients were	59.7±	139/	Mortality	30 days	Preoperativ	Preoperative
2018	control		undergoing	included if	14.1	169	Major		e anemia	anemia was
	study		elective abdominal	they met all the			complicatio			defined as
			surgery	following			ns			hemoglobin
				criteria:			Health			lower than
				1. Age greater			Related			12g/dL.
				than 18 years;			Quality of			
				2. Diagnosis of			Life 30			
				a solid			days after			
				neoplasm, plan			surgery			
				for elective			ICU length			
				open			of stay			
				abdominal			Hospital			
				surgery with			length of			
				curative intent			stay			
				or bowel						

reconstruction
from previous
primary tumor
excision;
3. Written
informed
consent.

Tavazzi 2006	Cohort study	2807	Acute heart failure	NR	73± 11	1698/ 1109	In-hospital all-cause mortality	NR	Anemia	According to the World Health Organization criteria, a hemoglobin concentration <13g/dL in men and < 12g/dL in
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									women	
Uscinsk a 2015	Cohort study	392	Critically ill cardiac patients	Critically ill cardiac patients who prospectively admitted to an intensive cardiac care unit.	70± 13.8	223/ 169	In-hospital mortality	NR	Anemia Hemoglobi n total	Anemia was defined according to the criteria of the World Health Organization (WHO), i.e. Hb level<12 g/dL in women and <13 g/dL in men.
Wang 2012	Cohort study	40	Mechanically ventilated patients (Acute exacerbation of COPD,	1. Invasive mechanical ventilation time >72h; 2. Hemoglobin	78.5± 9.4	23/17	Length of ICU stay Length of hospital stay	NR	Anemia	Anemia was defined as Hb level<100g/L.

			pneumonia, septic shock, acute left heart failure and others which need Mechanical ventilation.)	≥100g/L before admission to intensive care unit;			ICU Mortality			
				3. Patients who are more than 18 years old.						
Younge 2012	Cohort study	5304	Acute coronary syndrome	All patients 18 years of age admitted with a first admission for ST-segment elevation myocardial infarction or	61± 12	3872/1432	30-day mortality	20 years	Anemia	Anemia was defined as hemoglobin < 13g/dL for men and <12g/dL for women.

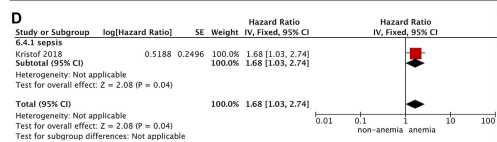
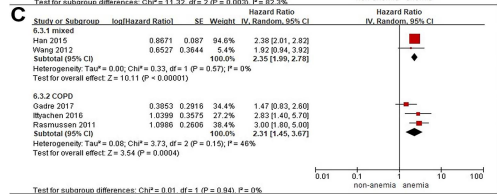
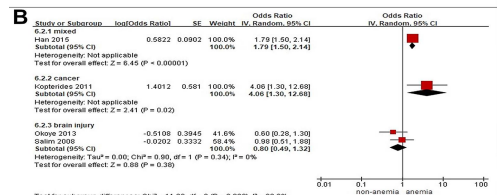
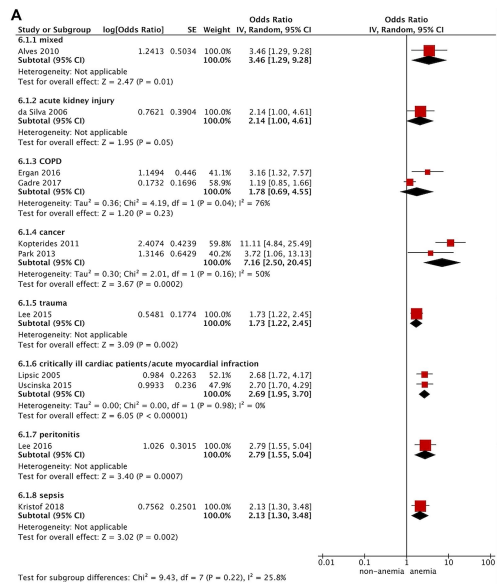
non-ST-segme
nt elevation
myocardial
infarction.

Supplemental table S2: Risk of bias assessment

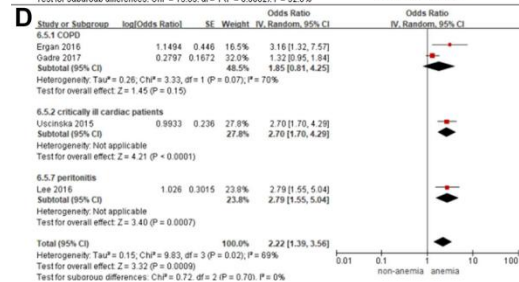
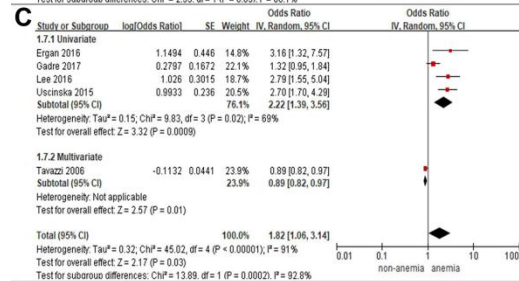
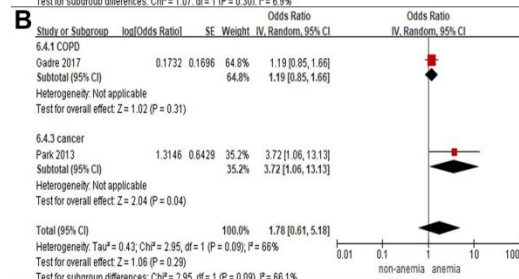
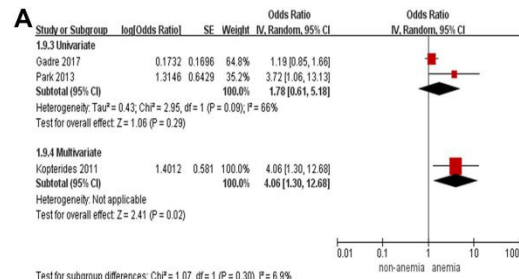
Study	Risk of bias	Study participants	Study attrition	Prognostic factor measurement	Outcome assessment	Study confounding	Statistical analysis and reporting
Alves 2010	High	High	Low	Low	Low	Low	High
Ameloot 2015	High	High	Low	High	High	Low	Low
da Silva 2006	High	High	Low	High	Low	High	High
Ergan 2016	High	High	Low	Low	Low	Low	Low
Gadre 2017	High	High	Low	Moderate	Low	Low	Low

Hamilton 2015	High	High	Low	Moderate	Moderate	Low	Low
Han 2015	High	Low	Low	High	Low	Low	Low
Ittyachen 2016	High	High	Moderate	Low	Low	Low	Low
Kopterides 2011	High	High	Moderate	Moderate	Low	Low	Low
Kristof 2018	High	High	Low	Low	Low	Low	Low
Kurtz 2010	High	High	Moderate	High	Low	Low	Low
Lee 2015	High	Low	Low	High	Low	High	High
Lee 2016	High	High	Low	High	Low	Low	Low
Lipsic 2005	High	High	Low	High	Low	Low	Low
Mohammadi 2018	High	Low	Low	High	Low	Low	Low
Mora 2014	High	High	Low	High	High	High	High
Mukhopadhyay 2014	High	Low	Low	High	Low	Low	Low
Ocal 2016	High	High	Low	Moderate	Low	Low	Low

Okoye 2013	High	High	Low	Moderate	Low	Low	Low
Park 2013	High	High	Low	Low	Low	Low	Low
Powell 2016	High	High	Low	High	Low	Low	Low
Rasmussen 2011	High	High	Low	Low	Low	Low	Low
Salim 2008	High	High	Low	Low	Low	Low	Low
Simoes 2018	High	High	Low	Low	Low	Low	Low
Tavazzi 2006	High	High	Low	Low	Low	Low	Low
Uscinska 2015	High	High	Low	Moderate	Low	High	High
Wang 2012	High	Moderate	Low	Moderate	Low	High	High
Younge 2012	High	High	Low	Moderate	Low	Low	Low



Supplemental Figure S1. Forest Plots Representing Anemia and All-Cause Mortality. univariate OR, subgrouped by diagnoses (A); multivariate OR, subgrouped by diagnoses (B); univariate HR, subgrouped by diagnoses (C); multivariate HR, subgrouped by diagnoses (D); OR, odds ratio; HR, hazard ratio.



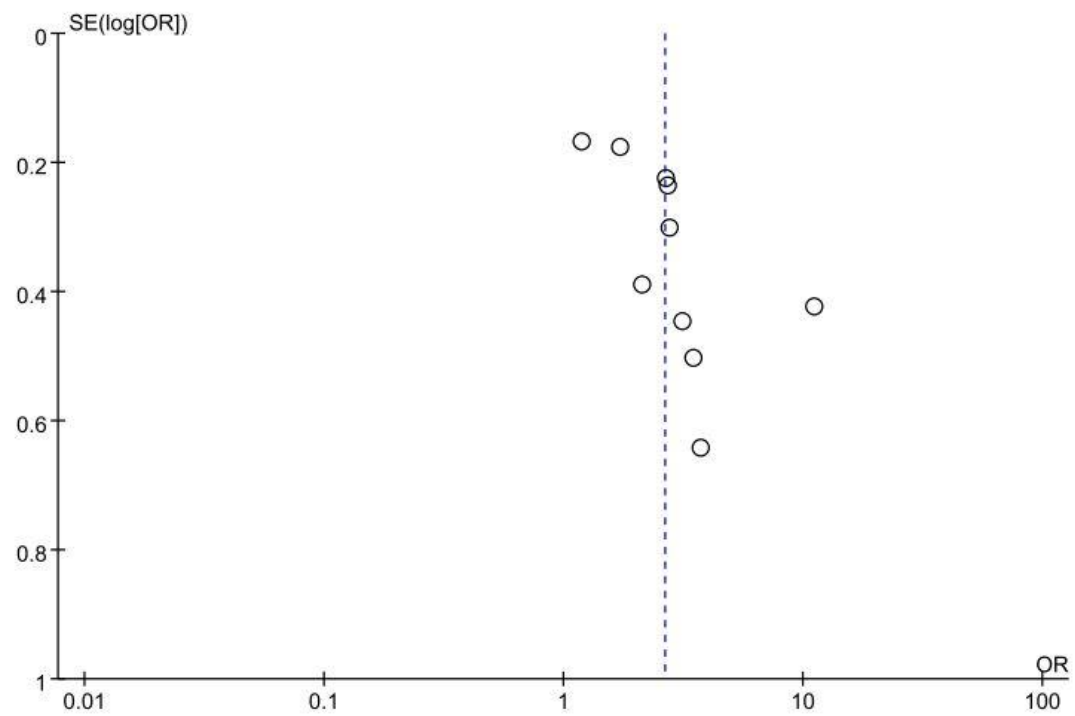
Supplemental Figure S2. Forest Plots Representing Anemia and Hospital/ICU Mortality. Odds ratios for anemia measured at admission and ICU mortality (A); anemia and ICU mortality, subgrouped by diagnoses (B); anemia and hospital mortality (C); anemia and hospital mortality, subgrouped by diagnoses (D).

Supplemental table S3: Study of anemia on admission and other complications

Study ID	Sample size	Risk factor	Outcome	Result data
Hamilton 2015	140	Anemia	Ventilation days	MD: 6.00, 95% CI (-0.98, 12.98)
Hamilton 2015	952	Anemia	ICU days	MD 1.02,95% CI (-8.59, 10.63)
Okoye 2013	812	Anemia	Hospital days	MD 14.7, 95% CI (-8.0, 37.40)
Powell 2016	210	Anemia	Progression from acute kidney injury I to acute kidney injury III	OR:1.40, 95% CI (0.69, 2.83)
Han 2015	2145	Anemia	Acute kidney injury (univariate)	OR:2.43, 95% CI (1.92, 3.07)

Han 2015	2145	Anemia	Acute kidney injury (multivariate)	HR:1.76, 95% CI (1.35, 2.30)
Mohammadi 2018	900	Anemia	Acute kidney injury (6 month after-multivariate)	OR:1.70, 95% CI (0.97, 2.98)
Han 2015	2145	Anemia	Early acute kidney injury (univariate)	OR:1.86, 95% CI (1.53-2.27)
Han 2015	2145	Anemia	Early acute kidney injury (multivariate)	HR:1.42, 95% CI (1.13-1.79)
Han 2015	2145	Anemia	Late acute kidney injury (univariate)	OR:2.53, 95% CI (1.73-3.70)
Han 2015	2145	Anemia	Late acute kidney injury (multivariate)	HR: 1.83, 95% CI (1.19-2.82)
Han 2015	2145	Anemia	Non-recovered acute kidney injury(univariate)	OR: 1.91, 95% CI (1.54, 2.37)
Han 2015	2145	Anemia	Non-recovered acute kidney injury (multivariate)	HR: 1.64, 95% CI (1.30, 2.08)
Kristof 2018	435	Anemia	ICU days	MD 8.0, 95%

				CI (5.93-10.07)
				MD 1.0, 95%
Kristof 2018	435	Anemia	Days without mechanical ventilation	CI (0.04-1.96)
				MD 1.0, 95%
Kristof 2018	435	Anemia	Days without vasopressors	CI (-0.49-2.49)
				MD -1.0, 95%
Kristof 2018	435	Anemia	Days without renal replacement therapy	CI (-2.77-0.77)
				OR: 3.80, 95%
Kurtz 2010	34	Anemia	Acute kidney injury (univariate)	CI (1.50, 9.63)
				OR: 1.80, 95%
Mora 2014	1252	Anemia	Complications within 30 days (multivariate)	CI (0.92, 3.51)
				OR: 1.74, 95%
Salim 2008	1150	Anemia	Complications within 7.5 years (multivariate)	CI (1.14, 2.65)
				OR: 1.30, 95%
Okoye 2013	812	Anemia	Acute respiratory distress (multivariate)	CI (0.23, 7.50)
				OR: 0.80, 95%
Okoye 2013	812	Anemia	Sepsis	CI (0.17, 3.70)



Supplemental Figure S3. Publication bias test: Funnel plot for all-cause mortality.