SUPPLEMENTARY APPENDIX

Supplemental Table 1: Multivariable Adjustment in Included Studies

Study	Follow Up (Years)	Mean Age	Male (%)	Adjustment Variables In Regression model	Selection	Comparability	Outcome
Blair, 2011 [1]	0.8	65	1524 (75)	Admission renal parameter of interest (SCr, BUN, or eGFR), discharge or Day 7 renal parameter of interest (for the post-discharge analysis), age, NYHA functional class, beta-blocker use, systolic blood pressure, sodium, BUN, BNP, and NT-proBNP	★★★	★	★★★
Chawla, 2014 [2]	1.4	67	28158 (99)	Sex, African American race, age>80 years, mean eGFR during baseline, preadmission diabetes or hypertension, history of CAD, previous stroke, and baseline serum SAlb>3 g/dl.	★★★	★★	★★★
Choi, 2010 [3]	5.7	44	16997 (98)	Age, sex, race, eGFR category, albuminuria, CD4 count, hypertension, diabetes, hospitalization in the intensive care unit, calendar year, history of CVD and history of CHF.	★★★	★★	★★★
Damman, 2009 [4]	1.5	71	551 (63)	Age, sex, NYHA class, LVEF, treatment assignment, systolic and diastolic blood pressure, heart rate, haemoglobin levels, eGFR at baseline, the occurrence of WRF before the studied period, medical therapy, history of myocardial infarction/atrial fibrillation/diabetes/stroke/COPD/Hypertension/Peripheral artery disease/time since diagnosis of heart failure.	★★★	★★	★★★
Damman, 2014 [5]	3.8	72	1402 (39)	Age; sex; race; etiology of HF; New York Heart Association functional class; left ventricular ejection fraction; systolic and diastolic blood	★★★	★	★★★

				pressures; heart rate; history of myocardial infarction, hypertension, atrial fibrillation, stroke, and diabetes; baseline medical therapy (angiotensin-converting enzyme inhibitor, beta-blocker, diuretics, digoxin, and spironolactone); and measurement of N-terminal pro–B-type natriuretic peptide (NT-proBNP, logarithmically trans- formed)			
Gammelager, 2014 [6]	2.7	59	11793 (61)	Age, sex, other heart disease, other cerebrovascular disease, hypertension, peripheral vascular disease, diabetes, CKD, cancer, surgical status at ICU admission, and primary diagnosis during current hospitalization and medications.	★★★	★★	★★★
Giacoppo, 2015 [7]	1.0	63	7064 (74)	Age, sex, diabetes, creatinine clearance <60 mL/min, contrast volume (per 100 mL increase), randomization to bivalirudin, randomization to glycoprotein IIb/IIIa inhibitor history of hypertension, hyperlipidemia, anemia, previous percutaneous coronary intervention, and previous coronary artery bypass grafting.	★★★	★★	★★★
Goldberg, 2009 [8]	3.0	60	1554 (79)	Age, sex, estimated glomerular filtration rate (MDRD), previous diuretic therapy, history of hypertension, diabetes, smoking, previous myocardial infarction, presence of anterior infarction, Killip class, heart rate and blood pressure on admission, use of reperfusion therapy (thrombolytic therapy or primary angioplasty), medical therapy (angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers and beta-blockers), and left ventricular ejection fraction.	★★★	★★	★★★

Hansen, 2015 [9]	2.7	68	3342 (70)	Sex, age, smoking, BMI, history of ischemic peripheral disease, previous stroke, previous myocardial infarction, history of arrhythmias, diabetes mellitus, dyslipidemia, hyper tension, CCI, baseline creatinine, EuroSCORE, type of surgical procedure (valve, Coronary Artery Bypass Grafting (CABG), combined valve and CABG, others), and extra corporal circulation.	★★★	★	★★★
Holzmann, 2013 [10]	4.1	67	18631 (79)	Age, sex, preoperative eGFR, atrial fibrillation, diabetes mellitus, peripheral vascular disease and prior heart failure,	★★★	★★	★★★
James, 2011 [11]	1.6	64	10560 (71)	Age, sex, baseline serum creatinine, baseline eGFR, proteinuria, diabetes, hypertension, hyperlipidemia, heart failure, cerebrovascular disease, peripheral vascular disease, chronic pulmonary disease, liver disease, malignancy, current smoker, acute coronary syndrome, coronary vascular disease, LVEF, and procedures	★★★	★★	★★★
Jose, 2006 [12]	3.5	59	1544 (83)	Age, sex, baseline creatinine (1.0, 1.0 to 2.0, and 2.0 mg/dl), history of hypertension, history of diabetes, history of dyslipidemia, history of CHF, left ventricular ejection fraction, previous MI, use of diuretics, and treatment assignment.	★★★	★★	★★★
Kim, 2014 [13]	2.2	70	200 (67)	Age>70, female sex, LV systolic dysfunction, acute coronary syndrome, eGFR, shock, PCI for LM disease, required hemodialysis after PCI.	★★★	★	★★★
Lindsay, 2003 [14]	1.0	63	4009 (67)	Revascularization, prior PCI, prior MI, prior CABG, unstable angina, diabetes (age and sex removed after stepwise regression)	★★★	★	★★★
Metra, 2008 [15]	1.3	68	190 (60)	Age, sex, body mass index, systolic blood pressure, heart rate, NYHA class, serum	★★★	★	★★★

				haemoglobin, creatinine, BUN, and sodium, both on admission and at discharge, left ventricular (LV) ejection fraction (EF) and a restrictive pattern of LV filling at Doppler-echocardiography, treatment with intravenous vasodilator and/or inotropic agents during the hospitalisation, prescription of angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, beta-blockers, aldosterone antagonists, digoxin and/or furosemide at discharge, as well as daily furosemide doses during the hospitalisation and at discharge.			
Mielniczuk, 2009 [16]	2.0	60	2886 (76)	Age, male sex, CRP quartile, baseline eGFR as a continuous variable, total cholesterol, triglycerides, low-density lipoprotein (LDL), history of hypertension, peripheral vascular disease, diabetes, current smoking, previous MI, left ventricular (LV) dysfunction, index diagnosis, catheterization or percutaneous intervention (PCI) for index event, treatment randomization, history of diuretic use within 7 d of admission, new or increase in diuretics in the first 30 d, angiotensin converting enzyme (ACE) inhibitor use at discharge, and new ACE inhibitor use in first 30 days	★★★	★★	★★★
Narula, 2014 [17]	3.0	63	514 (76)	age, sex, diabetes mellitus, smoking, Killip class>1, LVEF, and anaemia	★★★	★	★★★
Olsson, 2013 [18]	4.1	67	18940 (79)	Age, sex, diabetes mellitus, estimated glomerular filtration rate, left ventricular ejection fraction, and myocardial infarction before surgery or during follow-up	★★★	★★	★★★

Ozrazgat-Baslanti, 2016 [19]	7	55	22828 (50)	Age, sex, ethnicity, charlson comorbidity index, hypertension, diabetes, chronic obstructive pulmonary disease, peripheral vascular disease, cerebrovascular disease, congestive heart failure, myocardial infarction, emergent surgery, surgery type, admission hemoglobin, and number of postoperative complications	★★★	★	★★★
Ryden, 2014 [20]	5.0	67	21962 (79)	Age, sex, diabetes mellitus, estimated glomerular filtration rate, left ventricular ejection fraction, prior MI, heart failure or stroke.	★★★	★★	★★★
Shirakabe, 2012 [21]	1.0	71	340 (68)	Age (> 72 years old, yes or no), type of HF (new onset or worsening), etiology of HF (ischemia or non- ischemia), sex (male or female), NYHA class (III or IV), blood urea nitrogen (> 21.4 mg/dL, yes or no), creatinine (> 1.11 mg/dL, yes or no), total bilirubin (> 0.60 mg/dL, yes or no), sodium (< 141 mmol/L, yes or no), potassium (> 4.20 mmol/L, yes or no), hemoglobin (< 12.7 g/dL, yes or no), C- reactive protein (< 0.55 mg/dL, yes or no), systolic blood pressure (SBP) (< 160 mmHg, yes or no), pulse (< 116 beats/minute, yes or no)	★★★	★★	★★★
Tsai, 2015 [22]	2.5	70	2230 (78)	Age, sex, diabetes, hypertension, chronic kidney disease, gout, dyslipidemia, atrial fibrillation, heart failure, malignancy, COPD, liver disease, high volume center, and medical center	★★★	★★	★★★
Uyarel, 2009 [23]	1.8	56	2091 (83)	Age, sex, diabetes, hypertension, chronic kidney disease, gout, dyslipidemia, atrial fibrillation, heart failure, malignancy, COPD, liver disease, high volume center, and medical center	★★★	★	★★★
Watabe, 2014 [24]	1.2	70	819 (77)	Age, sex, CKD, Killip Class, Peak CK>4000, and IABP	★★★	★	★★★

Wu, 2014 [25]	3.4	63	4976 (58)	Sex, Age, Charlson Score, CHF, Dementia, COPD, Rheumatological Disease, Hemiplegia, Tumor, DM, Moderate or severe liver disease, Chronic kidney disease, in-hospital comorbidity, and operative category	★★★★	★★	★★★

Supplemental Table 2: Subgroup Analysis for the Association Between Acute Kidney Injury and Cardiovascular Mortality

Stratification	Number of Studies	Relative Risk	95% CI	I2 (%)	P-value
CVD Mortality – Setting					
CIN	3	2.42	1.49-3.91	27	0.36
Other	2	1.59	1.16-2.19	0	
CVD Mortality – Median Proportion Baseline CHF (min-max)					
0.06; 0.05-0.06]	3	1.68	1.28-2.19	0	0.35
0.09; 0.06-0.11]	2	2.61	1.08-6.30	72	
CVD Mortality – Median Proportion Baseline CKD (min-max)					
0.10; 0-0.20]	2	2.61	1.08-6.30	72	0.38
0.66; 0.33-1]	2	1.71	1.24-2.36	0	

CVD is cardiovascular, CHF is congestive heart failure, and CIN is contrast induced nephropathy. There were insufficient studies to examine the prognostic significance of AKI by setting (Peri-operative or ICU), severity of AKI, recovery of renal function, and proportion of participants with baseline stroke and baseline ischemic heart disease. With respect to the analysis based on the proportion of participants with baseline IHD: in 5 of 6 studies, 100% of participants had baseline IHD, therefore not meeting our criteria for at least two studies in each strata.

Supplemental Table 3: Subgroup Analysis for the Association Between Acute Kidney Injury and Major Cardiovascular Events

Stratification	Number of Studies	Relative Risk	95% CI	I2 (%)	P-value
MACE – Setting					
Other	4	1.29	1.19-1.41	20	-
MACE – Median Proportion Baseline CHF (min-max)					
[0.10; 0.05-0.14]	3	1.52	1.10-2.08	70	0.63
[1; 0.15-1]	3	1.39	1.22-1.59	0	
MACE – Median Proportion Baseline IHD (min-max)					
[0.56; 0.54-0.71]	3	1.39	1.22-1.59	0	
[1; 1-1]	3	1.52	1.10-2.08	70	0.63
MACE – Median Proportion Baseline Stroke (min-max)					
[0.06; 0.02-0.06]	3	1.29	1.16-1.45	26	0.18
[0.08; 0.07-0.08]	2	1.68	1.17-2.42	50	

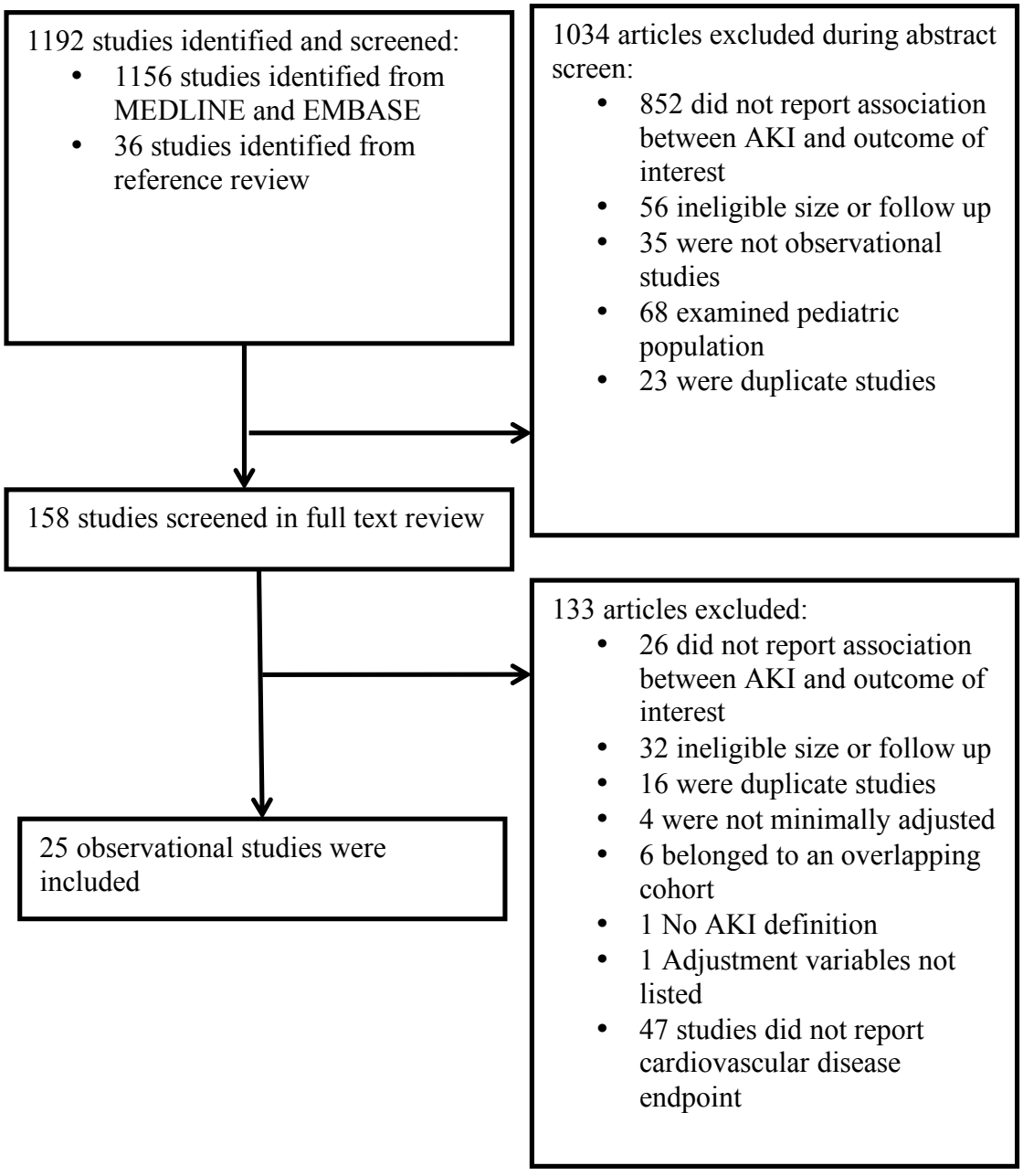
IHD is ischemic heart disease and CHF is congestive heart failure. There were insufficient studies to examine the prognostic significance of AKI by setting (contrast induced nephropathy and Peri-operative), severity of AKI, recovery of renal function and by the baseline proportion of adults with chronic kidney disease.

Supplemental Table 4: Subgroup Analysis for the Association Between Acute Kidney Injury and Stroke

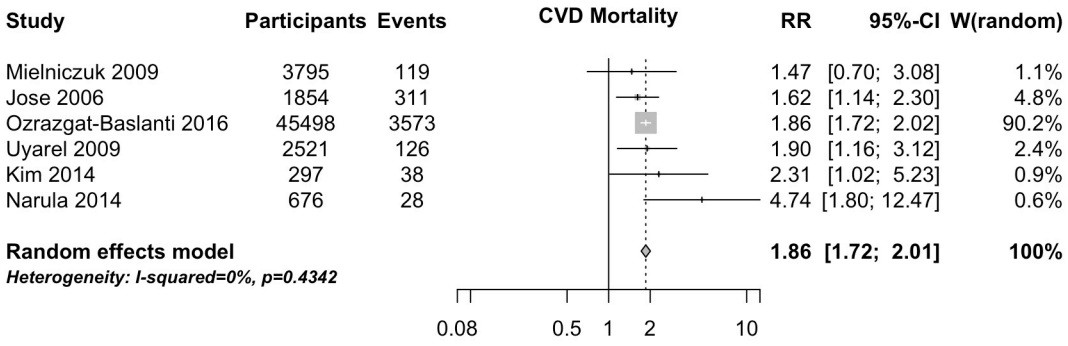
Stratification	Number of Studies	Relative Risk	95% CI	I2 (%)	P-value
Stroke – Setting					
Peri-operative	2	1.12	0.98-1.28	0	0.70
Other	2	1.24	1.01-1.51	0	
Stroke – Severity					
Mild AKI	3	1.18	1.02-1.36	0	0.91
Moderate to Severe AKI	3	1.20	0.90-1.60	0	
Stroke – Median Proportion Baseline CHF (min-max)					
[0.04; 0-0.05]	3	1.12	0.97-1.28	0	0.43
[0.13; 0.12-0.15]	2	1.23	1.02-1.48	0	
Stroke – Median Proportion Baseline IHD (min-max)					
[0.15; 0.12-0.72]	3	1.18	1.01-1.38	0	0.65
[1; 1-1]	2	1.13	0.97-1.31	0	
Stroke – Median Proportion Baseline Stroke (min-max)					
[0; 0-0]	3	1.16	1.04-1.29	0	0.73
[0.07; 0.06-0.07]	2	1.06	0.67-1.70	0	
Stroke – Median Proportion Baseline CKD (min-max)					
[0.11; 0.09-0.12]	2	1.19	1.01-1.41	0	0.61
[0.21; 0.19-0.24]	2	1.13	0.98-1.30	0	

IHD is ischemic heart disease. There were insufficient studies to examine the prognostic significance of AKI by setting (contrast induced nephropathy) and recovery of renal function.

Supplemental Figure 1: Identification of Included Studies

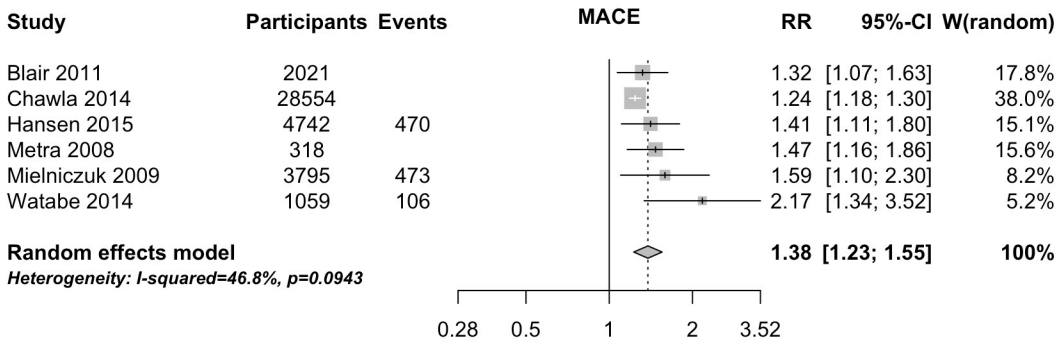


Supplementary Figure 2: Association between Acute Kidney Injury and Cardiovascular Mortality



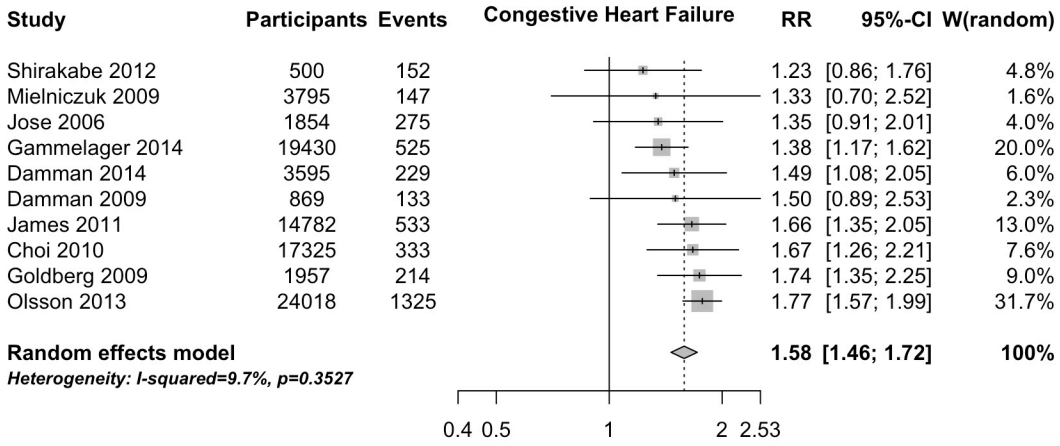
CVD is cardiovascular. Area of each square is proportional to the inverse variance of the estimate. Horizontal lines indicate 95% confidence intervals. W(Random) is the weight of each study.

Supplementary Figure 3: Association between Acute Kidney Injury and Major Adverse Cardiovascular Events



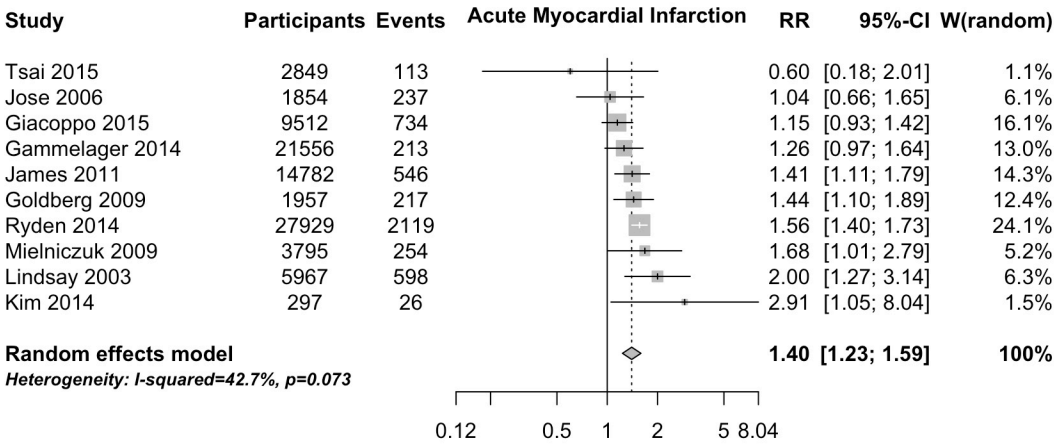
MACE is major adverse cardiovascular events. Area of each square is proportional to the inverse variance of the estimate. Horizontal lines indicate 95% confidence intervals. W(Random) is the weight of each study.

Supplementary Figure 4: Association between Acute Kidney Injury and Congestive Heart Failure



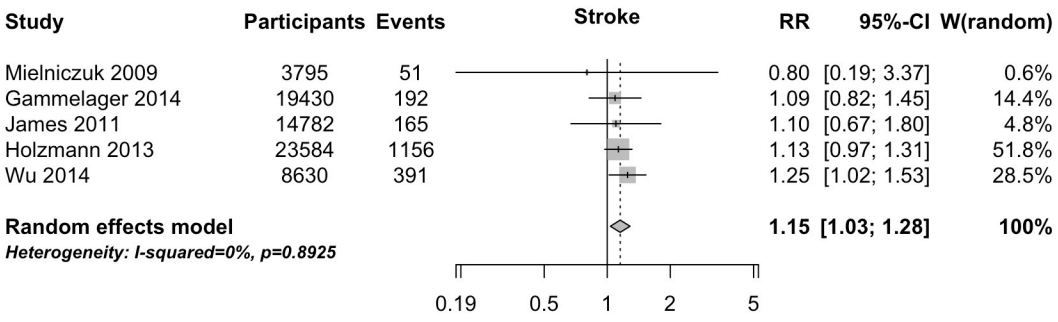
Area of each square is proportional to the inverse variance of the estimate. Horizontal lines indicate 95% confidence intervals. W(Random) is the weight of each study.

Supplementary Figure 5: Association between Acute Kidney Injury and Acute Myocardial Infarction



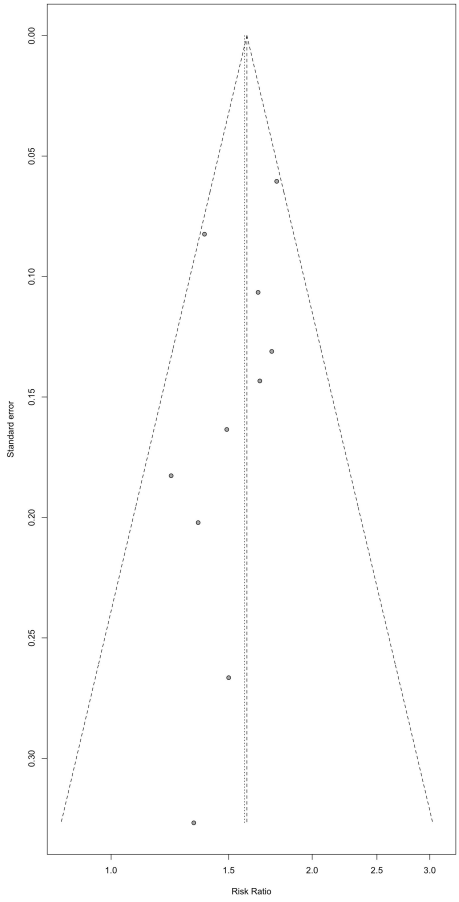
Area of each square is proportional to the inverse variance of the estimate. Horizontal lines indicate 95% confidence intervals. W(Random) is the weight of each study.

Supplementary Figure 6: Association between Acute Kidney Injury and Stroke

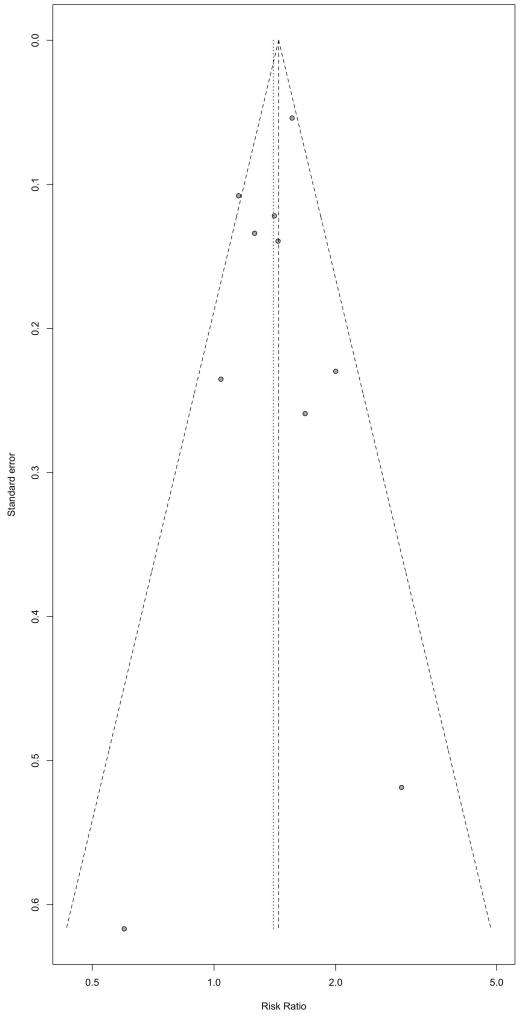


Area of each square is proportional to the inverse variance of the estimate. Horizontal lines indicate 95% confidence intervals. W(Random) is the weight of each study.

Supplemental Figure 7: Funnel Plot for the Association Between Acute Kidney Injury and Congestive Heart Failure



Supplemental Figure 8: Funnel Plot for the Association Between Acute Kidney Injury and Acute Myocardial Infarction



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