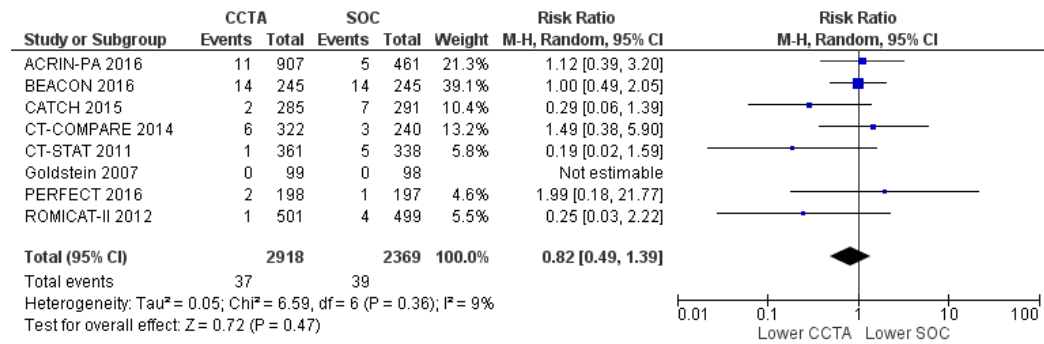


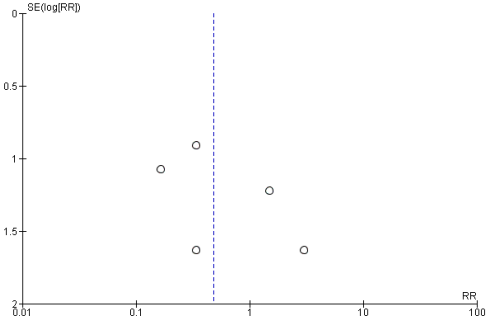
ONLINE SUPPLEMENT MATERIAL

Supplement figure 1. Myocardial infarction with coronary computed tomography angiography compared to other standard of care approaches in patients with acute chest pain. The size of central markers reflects the weight of each study.

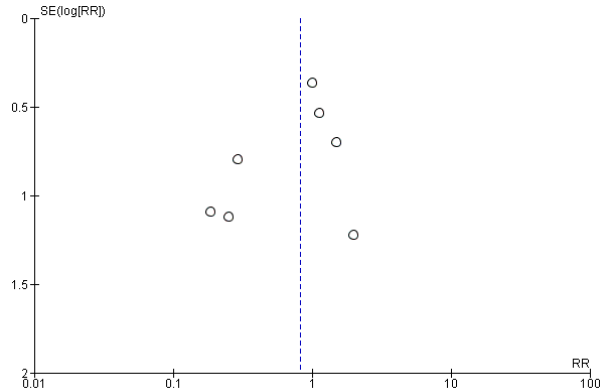


CCTA coronary computed tomography angiography, SOC standard of care.

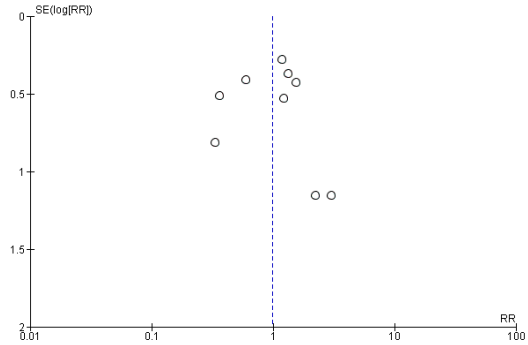
Supplement figure 2. Funnel plots for CCTA vs SOC for all-cause mortality.



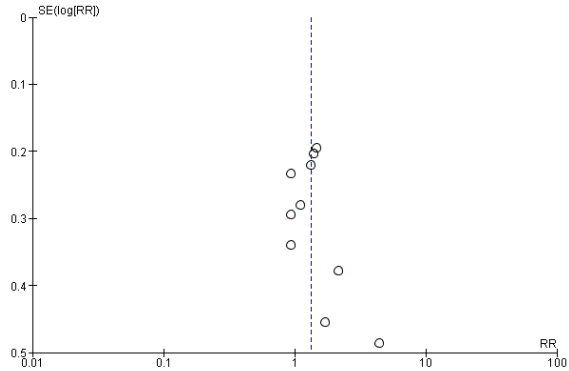
Supplement figure 3. Funnel plots for CCTA vs SOC for myocardial infarction,



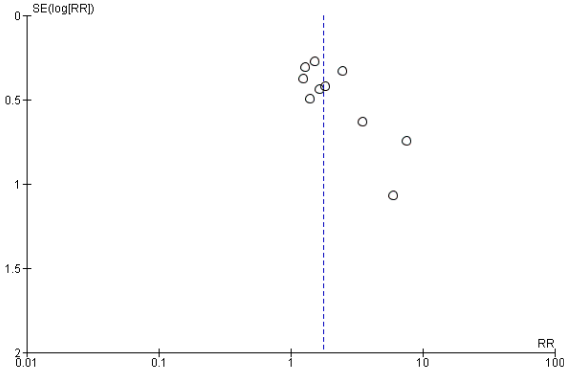
Supplement figure 4. Funnel plots for CCTA vs SOC for major adverse cardiovascular events,



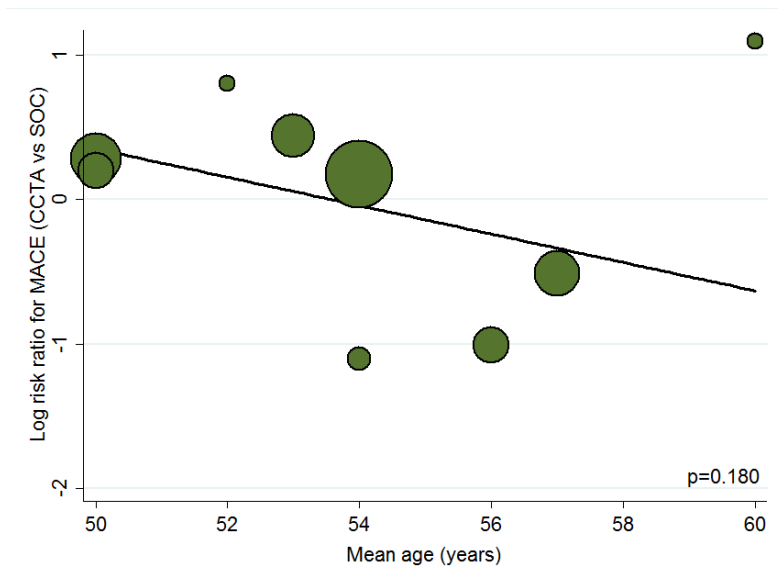
Supplement figure 5. Funnel plots for CCTA vs SOC for invasive coronary angiography.



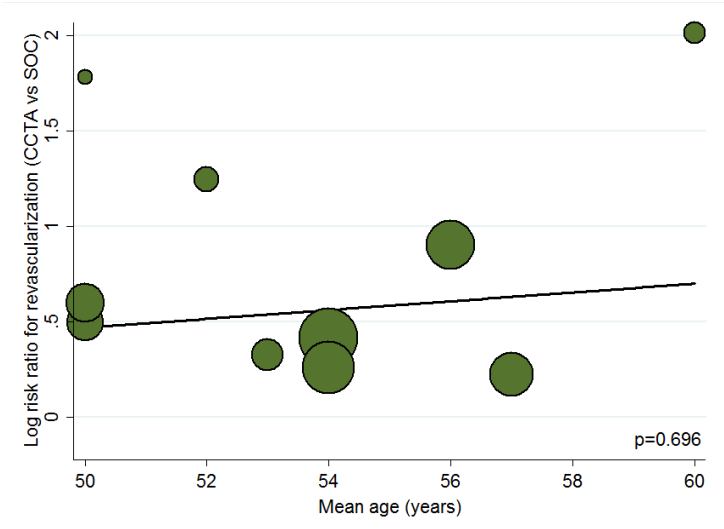
Supplement figure 6. Funnel plots for CCTA vs SOC for revascularization.



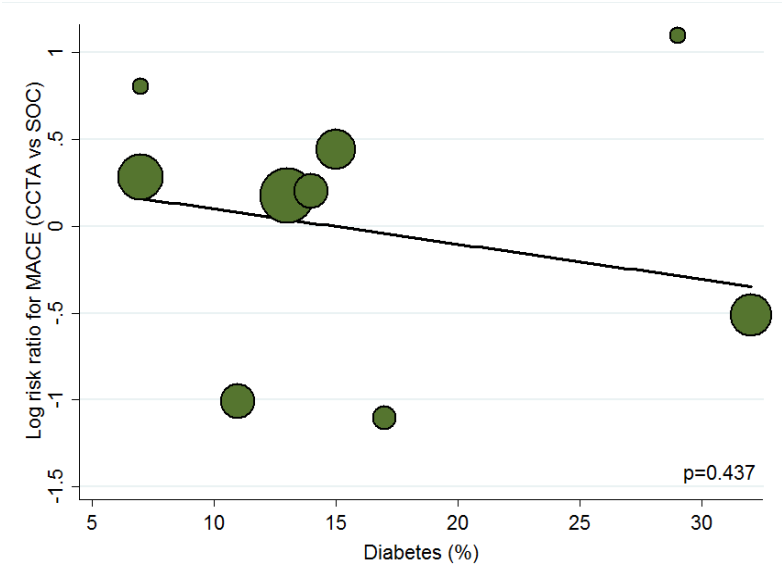
Supplement figure 7. Meta-regression MACE and age



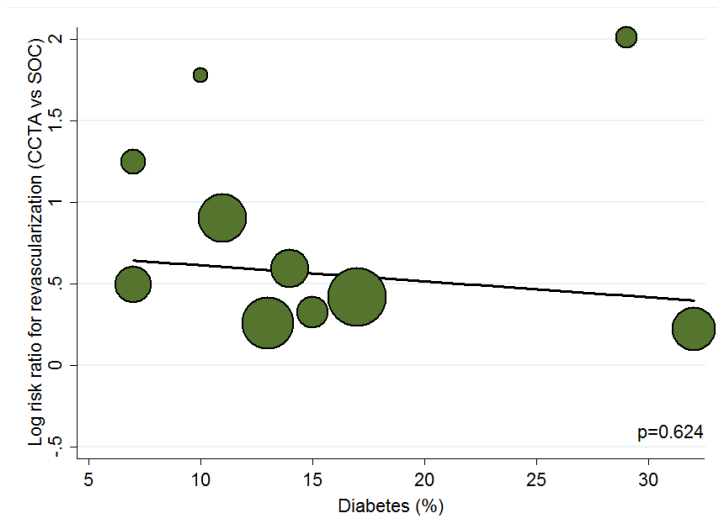
Supplement figure 8. Meta-regression revascularization and age



Supplement figure 9. Meta-regression MACE and diabetes



Supplement figure 10. Meta-regression revascularization and diabetes



Supplement table 1. Revascularization used in the included studies

| Study | Revascularization | |
|--------------------|-------------------|------|
| | PCI | CABG |
| ACRIN PA(7,8) | Not Reported | |
| BEACON(9) | Yes | Yes |
| CATCH(10,11) | Yes | Yes |
| CT-COMPARE(12) | Yes | Yes |
| CT-STAT(13) | Yes | Yes |
| Goldstein et al(4) | Yes | Yes |
| Nabi et al(14) | Not Reported | |
| PERFECT(15) | Yes | Yes |
| PROSPECT(16) | Yes | Yes |
| ROMICAT-II(17) | Yes | Yes |

CABG coronary artery bypass grafting surgery, PCI percutaneous coronary intervention

Supplement table 2. Inclusion and exclusion criteria of the trials*

| Study | Inclusion Criteria | Exclusion Criteria |
|--------------------|--|---|
| ACRIN PA(7,8) | Age >30 years, non-ischemic EKG, TIMI score 0-2 | Non-cardiac symptoms requiring admission, normal CCTA or ICA within 1 year |
| BEACON(9) | Age men 30-75 years and women 30-80 years, negative cardiac biomarkers | BMI >40 kg/m ² , non-cardiac symptoms, need for urgent ICA, clinical instability |
| CATCH(10,11) | Age >18 years, non-ischemic EKG, negative cardiac biomarkers, planned for discharge within 24hrs | Prior CABG, mental or physical conditions impairing follow up, abnormal chest radiography |
| CT-COMPARE(12) | Non-ischemic EKG, negative cardiac biomarkers, TIMI score <4 | AF, severe reactive airway disease |
| CT-STAT(13) | Age >25 years, chest pain during the past 12 hrs, non-ischemic EKG, negative cardiac biomarkers, TIMI score ≤4 | LVEF <45%, AF or markedly irregular rhythm, BMI >39 kg/m ² |
| Goldstein et al(4) | Age >25 years, chest pain during the past 12 hrs, non-ischemic EKG, negative cardiac biomarkers, low likelihood of infarction or complications | LVEF <45%, AF or markedly irregular rhythm, BMI >39 kg/m ² |

| | | |
|----------------|--|---|
| Nabi et al(14) | Age > 18 years, negative cardiac biomarkers, hospitalized for chest pain awaiting MPI | LVEF <45%, underlying comorbidity limiting follow up, duplicate emergency room visits, patient/physician refusal to participate |
| PERFECT(15) | Age > 45 years, non-ischemic EKG, negative cardiac biomarkers | AF or markedly irregular rhythm |
| PROSPECT(16) | Non-ischemic EKG, negative cardiac biomarkers | CCTA, MPI, or ICA within 6 months |
| ROMICAT-II(17) | Age 40-74 years, chest pain that lasted >5 min and <24hrs, non-ischemic EKG, negative cardiac biomarkers | BMI >40 kg/m ² , symptomatic asthma, non-sinus rhythm |

*Uniformly accepted exclusion criteria include pregnancy, renal failure, allergy to iodine contrast, and inability to obtain informed consent

AF atrial fibrillation, BMI body mass index, CABG coronary artery bypass grafting surgery, CCTA coronary computed tomography angiography, EKG electrocardiogram, ICA invasive coronary angiography, MPI myocardial perfusion imaging, LVEF left ventricular ejection fraction, TIMI Thrombolysis in Myocardial Infarction.

Supplement table 3. Repeat emergency department visits and hospitalizations in the included trials

| Study | Follow-up, months | Repeat ED visits | | | Repeat Hospitalization | | |
|--------------------|-------------------|------------------|-------|---------|------------------------|-------|---------|
| | | CCTA | SOC | P value | CCTA | SOC | P value |
| ACRIN PA(7,8) | 12 | 36% | 38% | N/A | 16% | 17% | N/A |
| BEACON(9) | 1 | 5% | 8 % | 0.27 | 3% | 6% | 0.12 |
| CATCH(10,11) | 19 | N/A | N/A | N/A | 10% | 12% | 0.23 |
| CT-COMPARE(12) | 12 | 12.7% | 10.0% | 0.3 | 10.3% | 10.8% | 0.8 |
| CT-STAT(13) | 6 | 0.6% | 1.3% | 0.43 | 0 | 0 | N/A |
| Goldstein et al(4) | 6 | 8.1%* | 8.1%* | 1.0 | 1% | 4.1% | 0.21 |
| Nabi et al(14) | 7 | N/A | N/A | N/A | N/A | N/A | N/A |
| PERFECT(15) | 12 | N/A | N/A | N/A | 14% | 16% | 0.5 |
| PROSPECT(16) | 12 | 63% | 57.5% | 0.31 | 43% | 49% | 0.27 |
| ROMICAT-II(17) | 1 | 2.8% | 3.8% | 0.38 | 1.4% | 1.4% | N/A |

*=emergency department and office visits

ED emergency department, CCTA coronary computed tomography angiography, SOC standard of care

Supplement table 4. Length of stay in the included trials

| Study | CCTA, hours | SOC, hours | P value |
|--------------------|---------------------------------------|---|----------------|
| ACRIN PA(7,8) | Median 18(7.6-27.2) | Median 24.8 (19.2-30.5) | N/A |
| BEACON(9) | Median 6.3 (4.8–11.1) | Median 6.3 (4.5–25.5) | 0.80 |
| CATCH(10,11) | N/A | N/A | N/A |
| CT-COMPARE(12) | Median 13.5 (11.2–15.7) | Median 19.7 (17.3–22.0) | 0.003 |
| CT-STAT(13) | N/A | N/A | N/A |
| Goldstein et al(4) | N/A | N/A | N/A |
| Nabi et al(14) | Mean 19.7±27.8 | Mean 23.5±34.4 | 0.002 |
| PERFECT(15) | Mean 48±40 | Mean 49±48 | 0.80 |
| PROSPECT(16) | Median 28.9 (11.0–48.4) | Median 30.4 (23.9–51.3) | 0.057 |
| ROMICAT-II(17) | Mean 23.2±37 Median 8.6 (6.4-27.6) | Mean 30.8±28 Median 26.7 (21.4-30.6) | <0.001 |

CCTA coronary computed tomography angiography, SOC standard of care

Supplement table 5. Cost of acute care in the included trials

| Study | CCTA cost | SOC cost | P-Value |
|--------------------|--|--|----------------|
| ACRIN PA(7,8) | N/A | N/A | N/A |
| BEACON(9) | Median €337 (337–932) | Median €511 (309–916) | <0.01 |
| CATCH(10,11) | N/A | N/A | N/A |
| CT-COMPARE(12) | Median \$2,193 (1,997–2,389) | Median \$2,704 (2,555–2,853) | <0.001 |
| CT-STAT(13) | Median \$2,137 (1,660–3,077) | Median \$3,458 (2,900–4,297) | <0.0001 |
| Goldstein et al(4) | Median \$1,586 (1,413–2,059) | Median \$1,872 (1,727–2,069) | <0.001 |
| Nabi et al(14) | Mean \$4,242±3,871 | Mean \$5,104±3,703 | 0.006 |
| PERFECT(15) | N/A | N/A | N/A |
| PROSPECT(16) | N/A | N/A | N/A |
| ROMICAT-II(17) | Median \$1,946 (1,514–4,164) Mean \$4,289±7,110 | Median \$2,809 (1,822–4,060) Mean \$4,060±5,452 | 0.65 |

CCTA coronary computed tomography angiography, SOC standard of care

Supplement table 6. Subgroup analysis comparing CCTA to SOC in patients evaluated in the emergency department.

| Outcome | Studies | Patients | Pooled RR (95% CI) | I² |
|-------------------------------|----------------|-----------------|----------------------------|----------------------|
| All-cause mortality | 6 | 4,316 | 0.76[0.21, 2.8], p = 0.68 | 0% |
| Myocardial Infarction | 6 | 4,316 | 0.90[0.53-1.55], p = 0.71 | 5% |
| MACE | 6 | 4,316 | 1.16[0.79, 1.71], p = 0.44 | 0% |
| Invasive Coronary Angiography | 6 | 4,316 | 1.36 [1.09, 1.69], p=0.006 | 0% |
| Revascularization | 6 | 4,316 | 1.64[1.20, 2.26], p=0.002 | 0% |

CI Confidence interval, MACE Major adverse cardiac events, RR Relative risk

Supplement table 7. Subgroup analysis comparing CCTA to SOC in the inpatient settings

| Outcome | Studies | Patients | Pooled RR (95% CI) | I² |
|-------------------------------|----------------|-----------------|---------------------------|----------------------|
| All-cause mortality | 3 | 1,371 | 0.21[0.04, 1.20], p=0.08 | 0% |
| Myocardial Infarction | 2 | 971 | 0.61[0.10, 3.81], p=0.60 | 42% |
| MACE | 4 | 1,959 | 0.83[0.38, 1.80], p=0.63 | 54% |
| Invasive Coronary Angiography | 4 | 1,959 | 1.35[0.82, 2.20], p=0.23 | 69% |
| Revascularization | 4 | 1,959 | 2.04[1.10, 3.76], p=0.02 | 48% |

CI Confidence interval, MACE Major adverse cardiac events, RR Relative risk

Supplement Table 8. Coronary computed tomography angiography compared to other standard of care approaches in the acute settings, fixed effects model.

| Outcome | Studies | Patients | Pooled RR (95% CI) | I² |
|-------------------------------|----------------|-----------------|-------------------------------|----------------------|
| All-cause mortality | 9 | 5,687 | 0.46 [0.18 – 1.18], p=0.11 | 0% |
| Myocardial Infarction | 8 | 5,287 | 0.79 [0.50 – 1.24], p=0.31 | 9% |
| MACE | 10 | 6,285 | 0.99 [0.74 – 1.32], p=0.93 | 26% |
| Invasive Coronary Angiography | 10 | 6,285 | 1.33 [1.13 – 1.57], p=0.0006 | 33% |
| Revascularization | 10 | 6,285 | 1.84 [1.44 – 2.36], p<0.00001 | 8% |

CI Confidence interval, MACE Major adverse cardiac events, RR Relative risk

Supplement Table 9. Coronary computed tomography angiography compared to other standard of care approaches in the acute settings, sensitivity analysis. Results after excluding BEACON trial are shown.

| Outcome | Studies | Patients | Pooled RR (95% CI)* | I² |
|-------------------------------|----------------|-----------------|------------------------------|----------------------|
| All-cause mortality | 8 | 5,197 | 0.38 [0.13 – 1.16], p=0.09 | 0% |
| Myocardial Infarction | 7 | 4,797 | 0.70 [0.33 – 1.47], p=0.35 | 19% |
| MACE | 9 | 5,795 | 0.92 [0.58 – 1.48], p=0.74 | 32% |
| Invasive Coronary Angiography | 9 | 5,795 | 1.33 [1.04 – 1.70], p=0.02 | 40% |
| Revascularization | 9 | 5,795 | 1.88 [1.40 – 2.52], p<0.0001 | 7% |

*Excluded BEACON trial.

CI Confidence interval, MACE Major adverse cardiac events, RR Relative risk