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# Percutaneous Coronary Intervention versus Coronary Artery Bypass Grafting for left main coronary artery disease? A systematic review and meta-analysis of randomized controlled trials.

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**Abstract**

**Background**: It is not clear whether Percutaneous Coronary Intervention (PCI) is as effective and safe as Coronary Artery Bypass Grafting (CABG) for left main coronary artery disease. We aimed to perform a systematic review and meta-analysis of all randomized controlled trials (RCTs) that compared PCI and CABG in left main coronary disease.

**Methods:** We searched PubMed, EMBASE, Cochrane, Scopus and relevant references for RCTs (inception through, November 20, 2016 without language restrictions) and performed meta-analysis using random effects model. All-cause mortality, Myocardial infarction, revascularization rate, stroke, , major adverse cardiac and cerebrovascular events (MACCE) were the measured outcomes.

**Results:** 6 RCTs with a total population of 4700 were analyzed. There was no difference in all-cause mortality at 30-day, 1-year and 5-year (1.8% vs. 1.1%; OR 0.60; 95%CI 0.26-1.39;P=0.23;$I^2$=9%) follow up between PCI and CABG. CABG group had less MI at 5-year follow up than PCI (5% vs. 2.5%; OR 2.04; CI 1.30-3.19; P=0.002;$I^2$=1%). Revascularization rate favored CABG in 1-year (8.6% vs 4.5%; OR 2; CI 1.46-2.73; P<0.0001;$I^2$=45%) and 5-year (15.9% vs. 9.9%;OR 1.73; CI 1.36-2.20; P<00001;$I^2$=0%)follow up. Though stroke rate was

lower in PCI group at 1-year there was no difference in longer follow up. MACCE at 5-year favored CABG (24% vs. 18%; OR 1.45; CI 1.19-1.76; P=00001;$I^2$=0%). On subgroup analysis, MAACE was not different between two groups in low to intermediate Syntax group while it was higher for PCI group with high Syntax group.

**Conclusion:** PCI could be as safe and effective as CABG in a select group of left main coronary artery disease patients.

**Key words:** Left main disease, Percutaneous coronary intervention, Coronary artery bypass grafting, Drug eluting stent

## Background

About 5% of patients undergoing coronary angiography are found to have left main coronary artery(LMCA)disease(1). LMCA supplies around 70% myocardium in patients with right dominant type and 100% in patients with left dominant type(2); LMCA stenosis is therefore associated with higher mortality(3,4).Coronary artery bypass grafting (CABG) has been recommended as the standard of care for the management of most LMCA disease by both European and U.S guidelines(5,6). However, new drug-eluting stent (DES) have shown a low risk of sudden death or stent thrombosis in moderate and long-term follow-up after left main(LM) stenting (7–10). Consequently, application of DES to include left main coronary patients has increased recently. Many registry studies have shown that PCI might be feasible and safe option in left main coronary disease.(9,11–14)

European Society guidelines recommend PCI in patients with favorable LMCA disease without complex and diffuse lesion(15). The recommendation was based on the subset analysis of Synergy between PCI with Taxus and Cardiac Surgery (SYNTAX) trial(16) which included both LM and/or 3-vessel disease (3VD) patients. LM subset of SYNTAX showed no difference in the composite outcome of all-cause mortality, myocardial infarction (MI), stroke and revascularization between PCI and CABG in select group of patients. However, the study was underpowered for subset analyses.

Meta-analyses in the past have suggested that PCI is safe and durable option of revascularization for LMCA patients at long term follow up(3,17). But, these meta-analyses involved mostly non randomized observational single center studies. More randomized controlled trials with large LMCA population have been published since these meta-analyses. Therefore we sought to do the systematic review and meta- analysis on the role of PCI versus CABG for LMCA disease.

## Methods

### Data sources and search strategy

This review was constructed according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for systematic reviews and meta-analyses.(18) We searched Medline/PubMed, Embase, Scopus and the Cochrane Library for the publications. Databases were searched from inception to November 20, 2016 with keywords 'Left main coronary disease' OR 'Unprotected left main coronary disease' AND 'Percutaneous Coronary Intervention' OR 'Drug Eluting Stent' AND 'Coronary artery bypass graft' OR 'CABG' in various combinations. Search strategy did not include the MeSH term and it was adapted for

each database as necessary. In addition to the computer search we manually reviewed the reference list of all included studies and published reviews to complete the search. Search strategy, study selection and meta-analysis were guided by a written protocol. Two investigators (SPS and KD) independently performed the database search and agreed on the final study selection.

**Inclusion and exclusion criteria**

We included studies that meet all the of the following criteria- 1) randomized controlled studies comparing PCI and CABG for the revascularization of left main coronary disease; 2) a minimum follow up period of one year; 3) report of at least two of the outcomes of interest (All cause mortality, Myocardial infarction, stroke, revascularization) . We excluded abstracts without full text publications and non-randomized studies. Also excluded were abstracts from annual meeting as our protocol pre-specified inclusion of full text articles only.

**Data Extraction**

First, items for data collection and the methodology for event count extraction were standardized. Two authors (SPS and JK) extracted data from the selected studies in duplicate using a standardized data extraction table. Data were extracted on study characteristics (author, journal, year of publications, number of patients, study design, follow-up duration, inclusion/exclusion criteria, primary and secondary outcomes), patients' characteristics (age, sex, history of MI, PCI, CABG, comorbidities, Syntax score), stents type, type of CABG (on pump vs. off pump), antiplatelet regimen and outcomes of interest and adverse events. Events count for the primary and secondary outcomes were extracted as reported by the individual studies. Any disagreement was resolved by consensus.

**Major outcomes**

The primary endpoint of our meta-analysis was all-cause mortality.. Analyses were done at 30-day, 1-year and 5-year follow up. We also pooled data from 3-year study to the 5-year dataset and reported that outcome as outcome at ≥3years follow up. Secondary endpoints were MI, stroke and revascularization, major adverse cardiac or cerebrovascular events (MACCE), a composite of all cause mortality, MI, stroke and revascularization; MACCE according to SYNTAX score, and adverse events in PCI and CABG.

**Outcome definitions**

All cause mortality: Death by any cause during the study period.

MI: Definition of MI varied among studies. Though all the studies required increase in cardiac biomarkers (CKMB or troponin) plus ischemic symptoms or diagnostic EKG for diagnosis the timing of definitions and threshold of enzyme elevation were different.

Stroke: Any acute neurological deficit attributed to impairment of cerebral circulation that lasts for >24hrs is defined by Stroke. Two studies(19,20) required stroke verification by CT and/or MRI.

Repeat revascularization: any revascularization procedures done by PCI or CABG after index procedure.

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MAACE: A composite outcome of all-cause mortality, myocardial infarction, stroke and revascularization.

**Statistical analysis**

The meta-analysis was performed using a random effects model with the help of Review Manager (RevMan 5.2, Cochrane Collaboration, Nordic Cochrane Center, Copenhagen, Denmark) for statistical analyses. Categorical variables were pooled as an odds ratio (OR) with 95% confidence interval (CI). Crude events from each study were used to calculate the odds ratio with 95% confidence intervals when appropriate. The *P* value <0.05 (2 tailed) was considered statistically significant. Study heterogeneity was evaluated by Cochrane's Q and *I2* index. We used the Cochrane Collaborations' tool for assessing risk of bias in the individual studies. Any disagreements were resolved by discussion.

**Quality assessment**

We used the Cochrane Collaboration tool for assessing risk of bias to determine the quality of included RCTs. This tool assesses the risk of selection bias, performance bias, detection bias, attrition bias, reporting bias, and other bias. Each RCT is categorized on the basis of criteria determining the likelihood of potential threats to validity. Quality assessment was independently performed by 2 reviewers (SPS and KD).

## Results

### Description of individual studies

We retrieved 351 citations from electronic database and manual searches as shown in **Figure1**. After duplicate articles were removed, 328 full texts were assessed for eligibility. We reviewed 20 citations for full text articles; eight full text articles were included in the final analysis(16,19–25). Two of the included studies(16,25) are the sub-studies of the main studies(22,24) that reported outcomes at different follow up period. One of the included studies(22) is the left main coronary disease subset of the SYNTAX trial(26). SYNTAX trial included both three-vessel and left main disease patients..

All the included studies were published between 2008 and 2016. There were a total of 4700 patients included in the meta-analysis. All the patients included in the meta-analysis had unprotected left main coronary artery disease.PCI arm consisted of 2349 and CABG arm consisted of 2351 left main disease patients. Of the total, 2594 had 5 year of follow-up. Male constituted more than 70% of population. More than 70% of the patients were male.98.5% of PCI patients were implanted with DES [65% of patients received BMS in Buszman et al study(21)]. Dual antiplatelet (Aspirin and Clopidogrel or ticlopidine) were used for at least a year after PCI in all studies except for SYNTAX left main (16) where it was recommended for at least 6-month only. Aspirin was recommended lifelong in PCI patients in all the studies. Antiplatelet therapy was recommended as per the local institution policy or the choice of surgeon in CABG arm in most studies. 60% of CABG was on-pump type. Patient and study characteristics in the individual studies are shown in **Table 1A** and **Table 1B.**

**Primary outcome**

All-cause mortality

There was no difference in all-cause mortality between PCI and CABG arm at 30-day (1.8% vs. 1.1%; OR 0.60;95%CI 0.26-1.39;P=0.23;$I^2$=9%), one year (2.3% vs. 3.5%; OR 0.67;CI 0.43-1.06; P=0.09;$I^2$=0%) and five year (7.8% vs.8.3%;OR0.92;CI 0.69-1.24; P=0.6;$I^2$=9%) [**Figure 2**]. To increase the population for analysis we combined studies with 5 year follow up with 3 year follow up and reported that outcome as mortality at ≥3years . At ≥3years no difference in all-cause mortality was observed between two arms (7.6% vs. 7.1%; OR 1.06; CI 0.82-1.38; P=0.66; I2=22%) (**Figure 2**)

Secondary outcomes

Myocardial infarction

There was no difference in rate of MI between revascularization strategies by PCI and CABG 30-day (3.5% vs. 4.6%; OR 0.75;CI 0.53-1.06; P=0.1;$I^2$=0%) and one year of follow up (2.4% vs. 2.2%;OR 1.10;CI 0.67-1.82; P=0.71;$I^2$=0%)[**Figure3**]. However, at 5-year follow up revascularization with CABG was associated with low rate of MI (5% vs. 2.5%; OR 2.04;CI 1.30-3.19; P=0.002;$I^2$=1%)[Fig3]. But rate of MI did not differ between two groups when analysis was done for ≥3years.

Revascularization rate

30-day revascularization rate was not different between PCI and CABG group (0.9% vs. 1%;OR 0.65; CI 0.35-1.21; P=0.17;$I^2$=0%)[Fig4].CABG showed better outcome at 1-year (8.6% vs. 4.5%;OR 2; CI 1.46-2.73; P<0.0001;$I^2$=45%) and 5-year (15.9% vs. 9.9%;OR 1.73; CI 1.36-2.20; P<00001;$I^2$=0%)[**Figure 4**]. CABG was associated with low revascularization rate at ≥3years follow up as well (Fig4). Only two studies reported ischemia driven target vessel revascularization(20,25); pooled analysis from these studies did not reveal any difference between PCI and CABG.

Stroke

Revascularization by PCI was associated with low stroke rate at 30-day (0.3% vs. 1.1%; OR 0.40; CI0.16-0.98; P=0.05; $I^2$=0%) and 1-year (0.2% vs. 1.3%; OR 0.21;CI 0.07-0.63; P=0.005;$I^2$=0%)[**Figure 5**]. However, there was no difference in stroke outcome between 2 arms at 5-year (1.8% vs. 1.8%; OR 0.93;CI 0.24-3.64; P=0.002;$I^2$=74%)[Fig5]. No difference was seen at ≥3years of follow up [**Figure 5**].

**MACCE**No difference in MACCE between PCI and CABG was noted at 1 year (9.9%vs 8.7% ; OR 1.15; CI 0.88-1.51; P=0.31;$I^2$=0%)[**Figure 6**]. However, 5-year MACCE favored CABG over PCI (24% vs. 18%; OR 1.45; CI 1.19-1.76; P=00001; $I^2$=0%)[Fig7]. Benefit of CABG over PCI for MACCE was maintained on the analysis of pooled data from studies reporting ≥3years follow up. (**Figure 6**)

CABG had more adverse events than PCI. Increased incidence of major bleeding, renal failure, post procedure arrhythmia, infection and surgical site complication was seen in CABG arm. The details on the adverse events are listed on **Table 2**.

Subgroup Analysis

MACCE based on Syntax score (anatomic scoring system based on coronary angiogram that quantifies lesion complexity) was reported by three studies(16,20,25). CABG showed a trend towards favorable outcome in low and intermediate Syntax group but it failed to reach statistical significance (21.5% vs. 16.6%; OR 1.35; CI 0.98-1.85; P=006; $I^2$=41%)[**Figure 7**]. In the high syntax group CABG was shown to be beneficial than PCI (36.8% vs. 24.5%; OR 1.79; CI 1.22-2.64; P=0.003; I2=0%)[**Figure 7**]. We also did subgroup analysis based on the types of DES ($1^{st}$ generation versus $2^{nd}$ generation). It did not alter our main results.

Sensitivity analysis

We performed the sensitivity analyses by assessing the contribution of each study to the overall estimate from the pooled estimate and by excluding individual study one at a time and recalculating the pooled odds ratio for the remaining. It did not substantially change the pooled point estimate on any endpoints.

Qualities of studies

Assessment of risk of bias was conducted by investigating random sequence generation, allocation concealment, blinding, completeness of outcome data, and potential for selective reporting. We found no evidence of significant bias (**Figure 8**). There were high risk of performance bias as blinding of participants and personnel were not possible. Other biases were

of low risk. Publication bias was not assessed because the included number of RCTs was less than ten(27).

**Discussion**

Our meta-analysis involving six RCTs is the largest study on this topic. Wedid not find survival benefit of CABG at 30-day, 1-year, 5-year or at ≥3years follow up. Improved mortality outcome in PCI could be due to use of newer stents and techniques. Two largest studies ( representing >50% of the total population pooled for analysis) included in our meta- analysis used second generation DES [Biolimus in NOBLE(20) and Everolimus in EXCEL(19)] while others used first generation [Sirolimus in Budriot et al(23),PRECOMBAT(25) and Buszman et al(21), Paclitaxel in Syntax(16) ]. More than 75% patients underwent DES placement under IVUS .IVUS guided DES placement has been shown to decrease long term mortality rate for the LMCA stenosis when compared with conventional angiographic guidance(28,29).

CABG was associated with favorable outcome with low rate of MI at 5-year though there was no difference in MI between CABG and PCI at earlier follow up. The high rate of MI at 5-year in PCI group is driven by NOBLE trial. The reasons for this could be twofold. First NOBLE did not report on periprocedural MI. A surgical registry in the past has reported a high incidence of periprocedural myocardial infarction in LM patients undergoing CABG(30). Second, 87% of the PCI treatment in NOBLE involved LMCA bifurcation. PCI to LMCA bifurcation is technically demanding and has been associated with high rates of adverse clinical events(31). We found low repeat revascularization rate in CABG in long term follow up. Only two studies reported target vessel revascularization(TVR)(20,25); pooled analysis from these studies didn't reveal any difference in repeat revascularization between PCI and CABG. The high rate of repeat

revascularization could be secondary to the use of first generation DES in four of the included studies(21–23,25). In the study by Buszman (21) only 35% of PCI patients were treated with DES. In previous studies, second-generation DES implantation resulted in lower Major Adverse Cardiac Events compared with first-generation DESs, primarily because of lower target lesion and vessel revascularization rates(32). The other reason for low revascularization in CABG arm could be due to use of internal mammary artery (IMA) graft in the majority of the cases. IMA graft use during CABG has been proven to reduce the incidence of repeat revascularization(33) because of its resistance to development of atherosclerosis(34). Plus, >65% of our patients had involvement of the distal LMCA involvement. Distal lesion as been identified as a significant predictor of repeated revascularization(7).Though CABG was associated with lower rate of MI and repeat revascularization than PCI at 5-year it did not seem to translate into decreased mortality.

Strokes were significantly reduced in patients undergoing PCI at 1-month and 1-year. There was no difference in stroke rate at 5-year or at ≥3years. This finding is in contrast with other studies(3,35). This could be due to the acute occurrence of majority of strokes (within a month of index procedure) in the CABG arm [12/26(46%) in EXCEL(19), 2/2(100%) in Buszman et al(21), 4/7 (57%) in NOBLE(20)]. Budriot et al(23) didn't report on the outcome of stroke while SYNTAX left main substudy (16) and PRECOMBAT(25) reported only 1-year and 5-year rate. By one year 9/14(64%) strokes and 2/2(100%) have occurred in SYNTAX and PRECOMBAT respectively. Acute procedure related stroke is a well known complication of CABG. Patients with CAD undergoing CABG have a significantly higher risk of stroke than those treated with

PCI at 30 days(36).The late catch-up of strokes in PCI arm might be related to discontinuation of dual antiplatelet after a year in PCI group.

An advantage of CABG over PCI was seen in MACCE at ≥3years and 5-year but no difference was seen in 1-year. This was mostly driven by higher rate of revascularization and MI in the PCI arm. A previous meta-analysis of 17 trials involving PCI for LMCA identified distal lesion as the most significant predictor or overall major adverse cardiac events(7).

In the subgroup analysis PCI was however equally safe as CABG for MACCE in patients with a low to intermediate SYNTAX score (0-32). In the high SYNTAX group MACCE fell in favor of CABG. Long term MACCE based on SYNTAX score was reported by three studies(16,20,25). Only about 20% of left main patients in these studies had high SYNTAX score. Patients with high SYNTAX score treated by PCI have been shown to be at a high risk of adverse cardiac events in previous studies(37–39). We also conducted subgroup analysis on various outcomes based on the type of stent ($1^{st}$ generation versus $2^{nd}$ generation); it did not substantially change our results. Biolimus-eluting stent (BES) was used in NOBLE trial. BES uses abluminal bioresorbable polymer coating(40). It is currently approved and marketed outside of United States(41).

A recently published metaanalysis by Nerlekar et al showed similar results as ours(42). However, there are some key differences between these studies. Nerlekar et al did not include Buszman et al study. 65% of patients in Buszman et al were treated with bare metal stents(BMS). New-generation drug eluting stents (DES) is preferred treatment modality over BMS(5). However, there still remain patient sub-populations that may still benefit from BMS

implantations since their concomitant triple therapy, i.e. dual antiplatelet therapy (DAPT) and oral anticoagulation can be reduced to lower the risk of gastrointestinal or intracranial bleeding(43). In the recently published NORSTENT trial, rate of repeat vascularization and stent thrombosis were lower in DES group but these findings didn't translate into decreased rate of death, MI or stroke at 5 years when compared to BMS(44). So, we did analysis including the study by Buszman et al to make it more comprehensive and inclusive of general population.

Unlike recently published study our meta-analysis showed higher rate of MI in PCI group at 5 year. Nerlekar et al (42) pooled results from studies with different lengths of follow up (3-year and 5-year) and reported MI rate. However, when we did analysis by limiting only studies with 5-year follow up it showed beneficial effect of PCI in CABG group. This result is in keeping up with that of previous study. A meta-analysis of RCTs and observational studies in the past has also shown low incidence of non-fatal MI in favor of CABG(3).

Our meta-analysis has several limitations. Heterogeneity in definitions of myocardial infarction by individual studies, small number of RCTs, absence of blinding of treatment assignments, use of different types of DES, variable duration of follow up are some of the limitations. Plus, variable use of antiplatelet between two arms may have affected clinical outcomes. The other limitation is that most of the studies did not report on the percentage of bifurcation lesion and how they were treated (simple bifurcation treated with one-stent approach vs. complex bifurcation treated with two-stent approach). Previous study has shown favorable outcome for simple bifurcation lesion treated with one-stent approach(45).

## Conclusion

Our study shows that PCI can be a feasible and safe option for revascularization of LMCA patients with low to intermediate Syntax score. Future studies may need to focus on the role of PCI in patients with high Syntax score and in complex bifurcation lesions of left main coronary artery to find out the role of PCI in the whole spectrum of left main disease. The decision about appropriate revascularization for LMCA patients should be individualized factoring into their clinical and angiographic risk factors and their preference. Our meta-analysis provides the important understanding of the expected outcome of PCI or CABG for revascularization in LMCA patients.

**Disclosures:** The authors declare that there is no conflict of interest

**Authors' Contribution**

(1) Conception and design: SPS and KD

(2) Provision of study material: SPS and JK

(3) Collection and assembly of data: SPS and JS

(4) Data analysis and interpretation: All authors

(5) Manuscript writing: All authors.

(6) Final approval of manuscript: All authors

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| Study/Journal/Year | Number of patients | Follow up | Participating countries | Primary outcome | Inclusion criteria | Exclusion criteria |
|---|---|---|---|---|---|---|
| Stone et al/NEJM/2016 (EXCEL trial) (19) | P 948<br>C 947 | Primary outcome reported at 3 year (5-year follow up going on) | Asia, Australia, North and South America and Europe | whether PCI was non inferior to CABG with respect to composite endpoint of death from any cause, stroke or MI at 3 yrs | stenosis of LMCA of 70% or > or stenosis of 50% to <70% which is hemodynamically significant. Low-to-intermediate anatomical complexity of CAD as defined by site-determined syntax score 32 or < | PCI of left main trunk, non-left main trunk within last year, CABG before randomization |
| Morice et al/Circulation/2010 and 2014 (SYTAX left main subset)(23) | P 357<br>C 348 | 5 years | USA and Europe | the composite of MACCE at 1 yr which included composite of all cause death, CVA, MI and repeat vascularization | de novo LM and/or 3VD disease and 50% target vessel stenosis with stable or unstable angina. | Previous PCI, CABG, acute MI or need for concomitant cardiac surgery |
| Park et al/NEJM/2011 (PRECOMBAT trial)<br>Ahn et al/2015/JACC 5-year outcome of PRECOMBAT(26) | P 300<br>C 300 | 5 years | South Korea | MACCE( composite of death from any cause, MI, stroke, ischaemia driven target vessel revascularization) for 12-month period after randomization | patients with stable and unstable angina, silent ischaemia or NSTEMI with newly diagnosed unprotected stenosis of more than 50% of left main coronary artery as estimated visually | Previous PCI, CABG, stroke, EF<30% |
| Makikallio et al/Lancet/2016 (NOBLE trial)(20) | P 592<br>C 592 | 5 Years | Nordic and Baltic countries plus United Kingdom | composite of all-cause mortality, myocardial infarction, stroke and repeat revascularization (major adverse cardiac and cerebrovascular events (MACCE)) | CAD with visually estimated stenosis diameter >=50% or fractional flow reserve <=0.80 in left main artery ostium,mid shaft or bifurcation with no more than 3 additional complex lesions | STEMI within 24hr, too high risk of CABG or PCI, expected survival less than a year. |
| Boudriot et al/JACC/2011(24) | P 100<br>C 101 | 1 year | Germany | freedom from major adverse cardiovascular events which included death from any cause, MI and the need for repeat revascularization at 12months | 18-80yrs with stenosis>=50% of unprotected left main with or without additional multivessel CAD | MI <48hr, valvular heart disease requiring surgery, previous heart surgery, severe PAD, significant carotid stenosis, CKD requiring dialysis, overt CHF, limited life expectancy, contraindication to antiplatelet therapy |
| Buszman et al/JACC/2008(22) | P 52<br>C 53 | 5 years | USA | change in LVEF assessed by echo 1 yr after index intervention | >50% narrowing of unprotected left main with or w/o multivessel CAD with documented myocardial ischaemia suitable for both PCI and CABG, | Acute MI, total occlusion of left main, TIA within 3 months, renal dysfunction, antiplatelets contraindications |

Abbreviations: P=PCI, C=CABG, CAD=coronary artery disease, MACCE=major adverse cardiac and cerebral vascular events,LMCA=left main coronary artery,3VD=3-vessel disease, PAD=peripheral artery disease, TIA=transient ischaemic attack, CKD=chronic kidney disease, ( )= study reference number

| Study | Age | Male % | HTN % | DM % | Current Smoker% | Prior MI % | Prior PCI % | Prior CABG % | Prior TIA/Stroke % | EF % | Syntax score | Type of stent | No of stents | LMCA only% | IMA % | Distal LMCA lesion % |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| NOBLE (20) | P 66 C 66 | P 80 C 76 | P 65 C 66 | P15 C15 | P19 C22 | NA | P20 C20 | P1 C1 | NA | P 60 C 60 # | P22.5(7.5) C 22.4(8)* | II Gen (EES) | 1(1-2)# | NA | NA | P 81 C 81 |
| EXCEL (19) | P66 C 65 | P 76 C 77 | P 74 C 74 | P30 C28 | P 24 C 20 | P 18 C17 | P 18 C16 | NA | P 5 C 7 | P 57(9.6) C 57(9)* | Low (<=22) P 59% C61% Intermediate (23-32) P 40% C38% | II Gen (BES) | 2.4(1.5)* | P 17 C 18 | 99 | P 81.8 C 79.2 |
| SYNTAX LM subset (23) | P 65 C65 | P72 C75 | P66 C62 | P23 C25 | P18 C24 | P28 C25 | Excluded | Excluded | P 4 C 4 | >30% P 98% C 98% | P 29(13.5) C 30(12.7)* | I Gen (PES) | NA | P 12 C 14 | NA | P 56 C 52 |
| PRECOMBAT (26) | P 61 C 62 | P76 C77 | P54 C51 | P34 C 30 | P29 C27 | P4 C6 | P12 C 12 | NA | NA | P 61(8.3) C 60(8.5) * | (<22) P129 CABG 104 (>22) PCI 160 CABG 165 | I Gen (SES) | 2.7(1.4)* | P 9 C 11 | 94 | P 66 C 61 |
| Boudriot et al (24) | P66 C 69 | P72 C77 | P 82 C 82 | P 40 C 33 | P35 C28 | P 19 C 14 | NA | NA | NA | P 65(55-70) C 65(55-68)# | P 24(19-29) C 23(14.8-28)# | I Gen (SES) | NA | P 28 C 29 | 99 | P 74 C 69 |
| Buszman et al (LE MANS) (22) | P 60 C 61 | P 60 C 73 | P 75 C70 | P19 C17 | NA | P 36 C 32 | NA | NA | NA | NA | P 25(8.7) C24(6.8)* | I Gen (SES) | NA | P 13 C 6 | 72 | P 56 C 60 |

#median(IQR) * mean (std deviation), HTN=hypertension,DM=Dibetes mellitus, MI= myocardial infarction, TIA=transient ischemic stroke, EF=ejection fraction, LMCA=left main coronary artery, IMA=internal mammary artery, Gen=First generation,II Gen= Second generation, EES=everolimu- eluting stent, BES=biolimus-eluting stent,PES=paclitaxel-eluting stent, SES=sirolimus-eluting stent, NA= not available

| Study Name | Major bleeeding | Infection | Arrhythmia | Renal failure | Pulmonary embolism | Surgery for access site complication |
|---|---|---|---|---|---|---|
| EXCEL 2016 | PCI 11/948 CABG 37/957 | PCI 24/948 CABG 133/957 | PCI 20/948 CABG 154/957 | PCI 6/948 CABG 24/957 | | |
| NOBLE 2016 | PCI 1/592 CABG 23/592 | PCI 0/592 CABG 3/592 | NA | NA | PCI 1/592 CABG 1/592 | PCI 2/592 CABG 4/592 |
| SYNTAX | NA | NA | NA | NA | NA | NA |
| PRECOMBAT 2011 | NA | NA | NA | NA | NA | NA |
| Boudriot et al 2011 | NA | PCI 0/100, CABG 5/101 | PCI 3/100, CABG 19/101 | PCI1/100, CABG 1/101 | | PCI 0/100, CABG 2/101 |
| Buszman et al 2008 | NA | NA | PCI 3/52 CABG 5/53 | PCI 0/52 CABG 1/53 | NA | NA |

n/N=no of events/total population, PCI=Percutaneous coronary intervention, CABG=Coronary artery bypass grafting, NA=not available

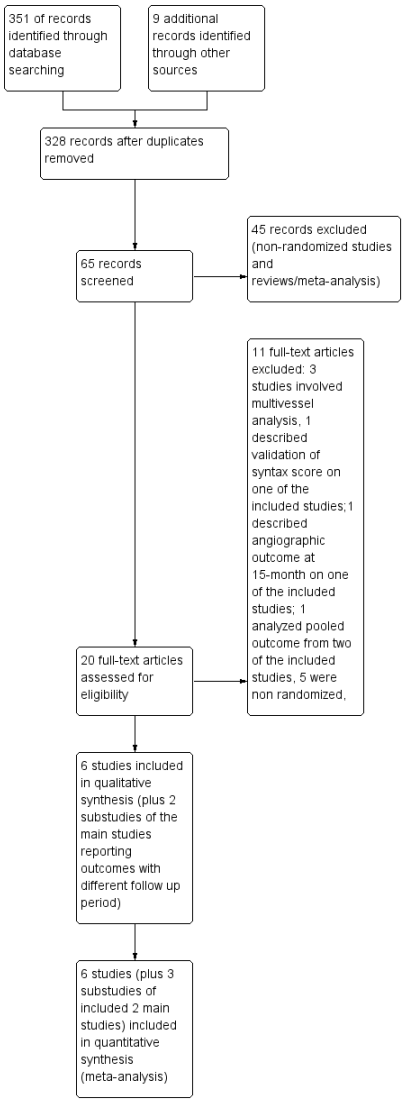


**Figure 1: Flow diagram of study**

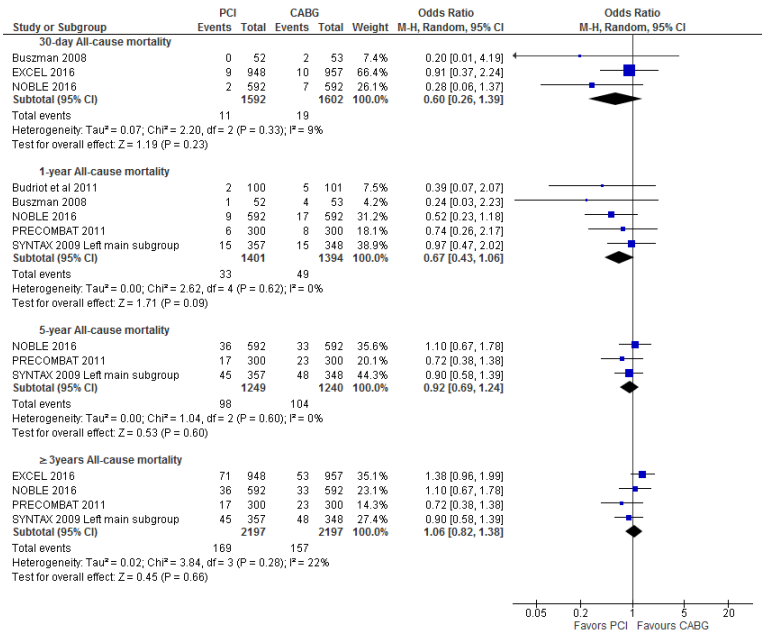


**Figure 2: Forest Plot of All-cause mortality in PCI and CABG for left main disease**

Forest plot showing odds ratio of All-cause mortality in PCI and CABG for left main disease at 30-day, 1-year, 5-year and ≥3years follow up
PCI=Percutaneous coronary intervention, CABG= Coronary artery bypass grafting

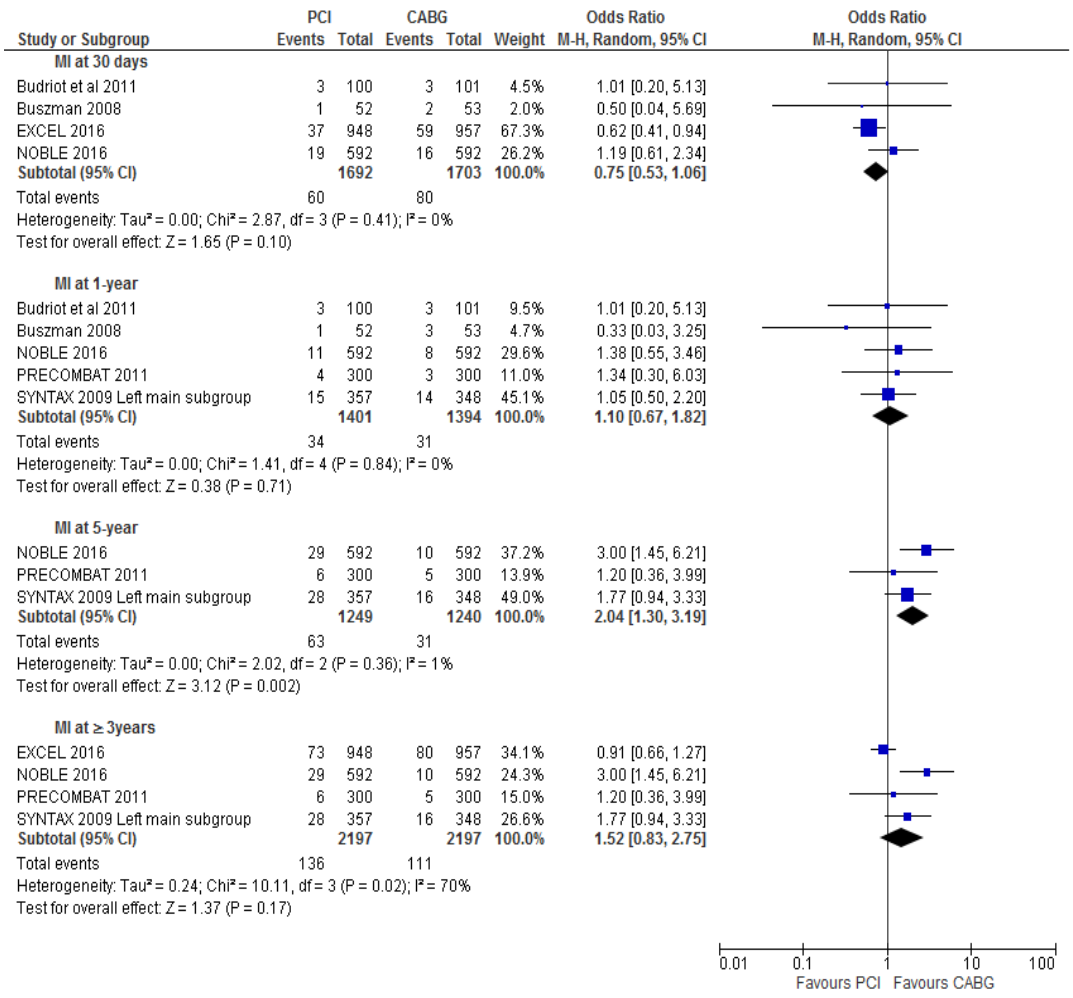


**Figure 3**: **Forest Plot of MI in PCI and CABG for left main disease**

Forest plot showing odds ratio of MI in PCI and CABG for left main disease at 30-day, 1-year, 5-year and ≥3years follow up
PCI=Percutaneous coronary intervention, CABG= Coronary artery bypass grafting, MI=Myocardial infarction

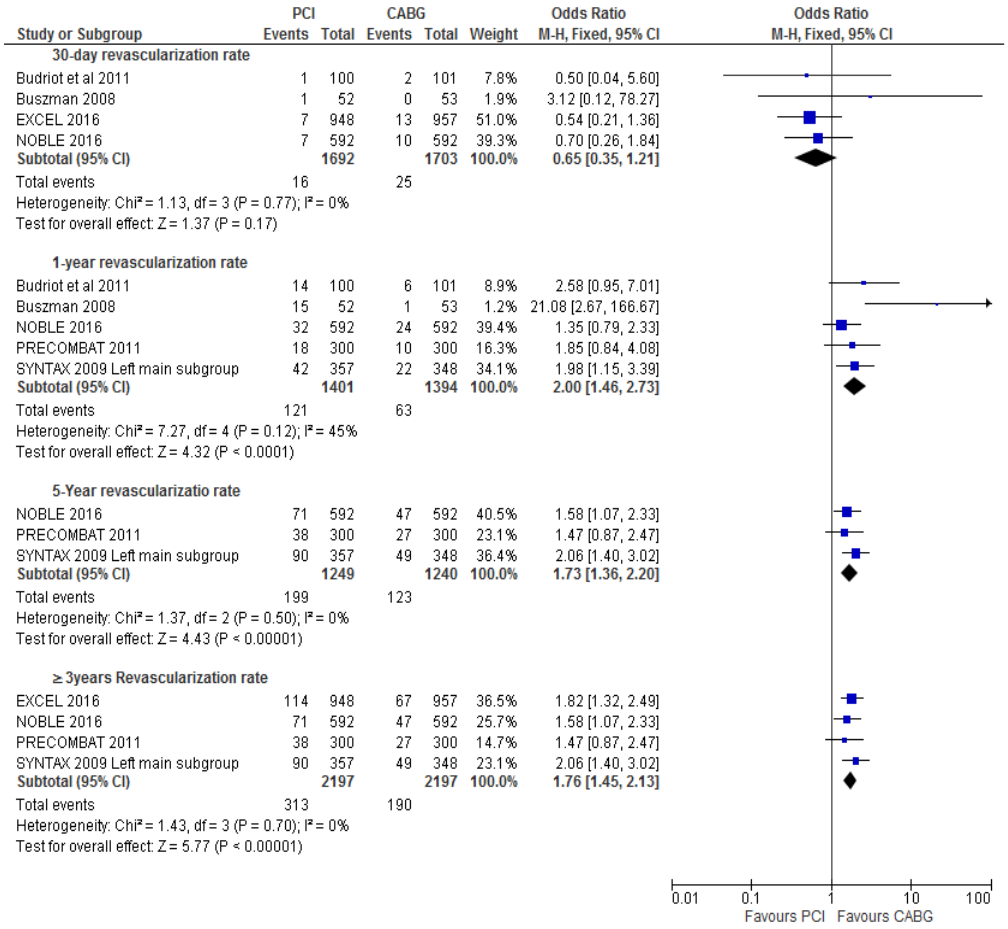


**Figure 4: Forest Plot of revascularization rate in PCI and CABG for left main disease**

Forest plot showing odds ratio of revascularization rate in PCI and CABG for left main disease at 30-day, 1-year, 5-year and ≥3years follow up
PCI=Percutaneous coronary intervention, CABG= Coronary artery bypass grafting

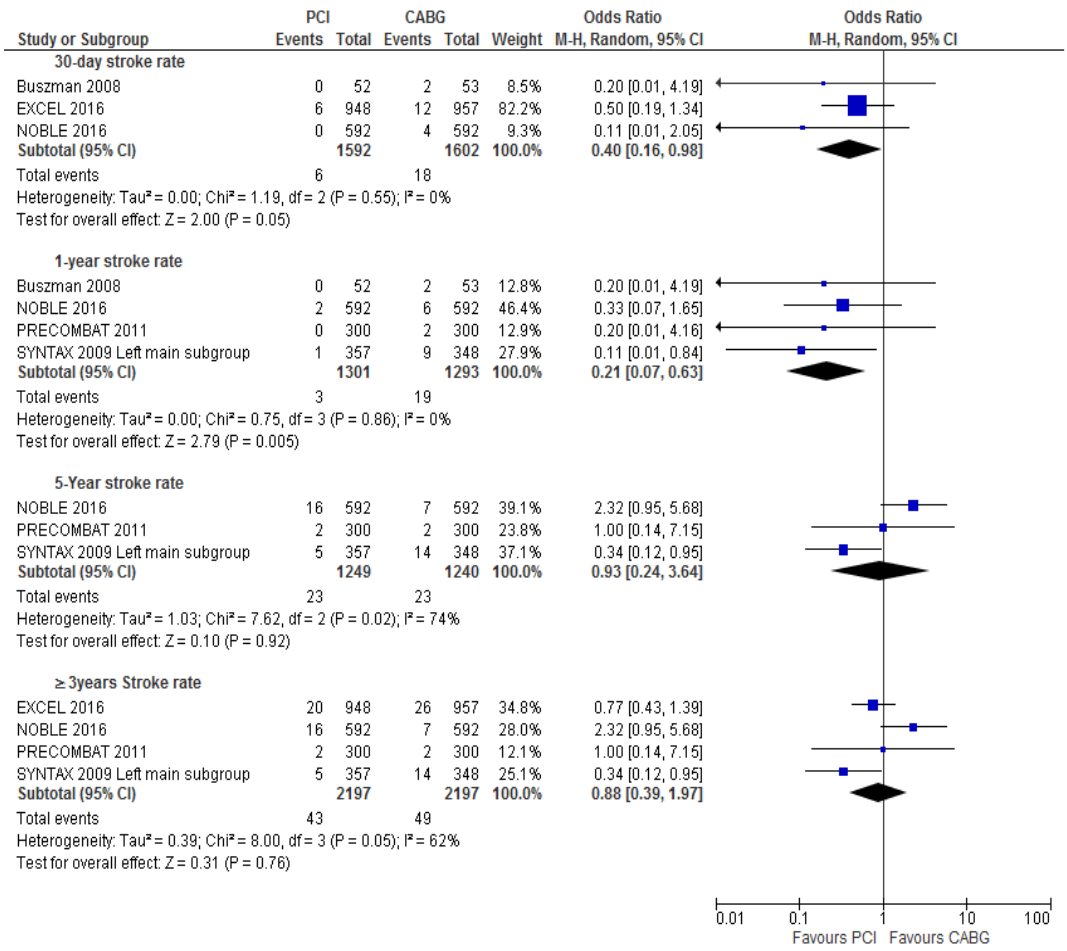


**Figure 5: Forest Plot of MI in PCI and CABG for left main disease**

Forest plot showing odds ratio of stroke in PCI and CABG for left main disease at 30-day, 1-year, 5-year and ≥3years follow up
PCI=Percutaneous coronary intervention, CABG= Coronary artery bypass grafting

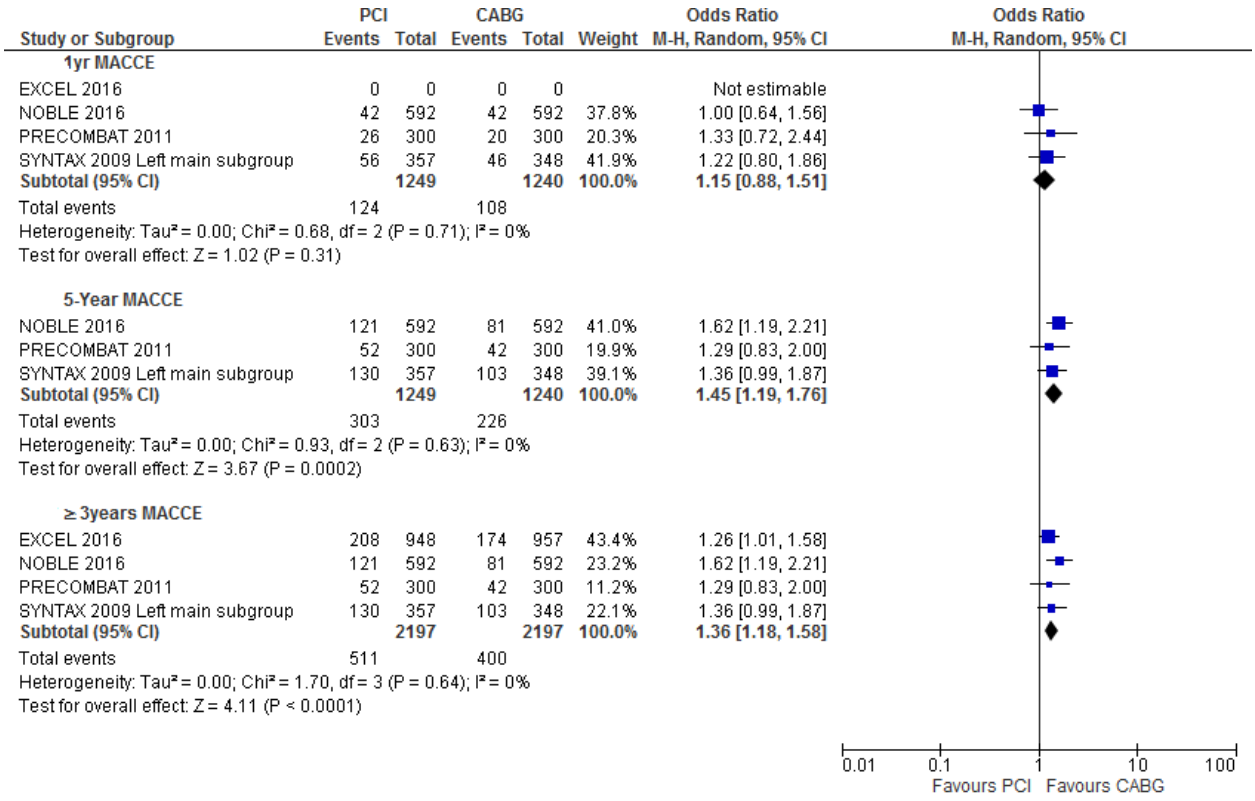


**Figure 6 : Forest Plot of MACCE in PCI and CABG for left main disease**

Forest plot showing odds ratio of MACCE in PCI and CABG for left main disease at 1-year, 5-year and ≥3years follow up PCI=Percutaneous coronary intervention, CABG= Coronary artery bypass grafting, MACCE=Major adverse cardiac and

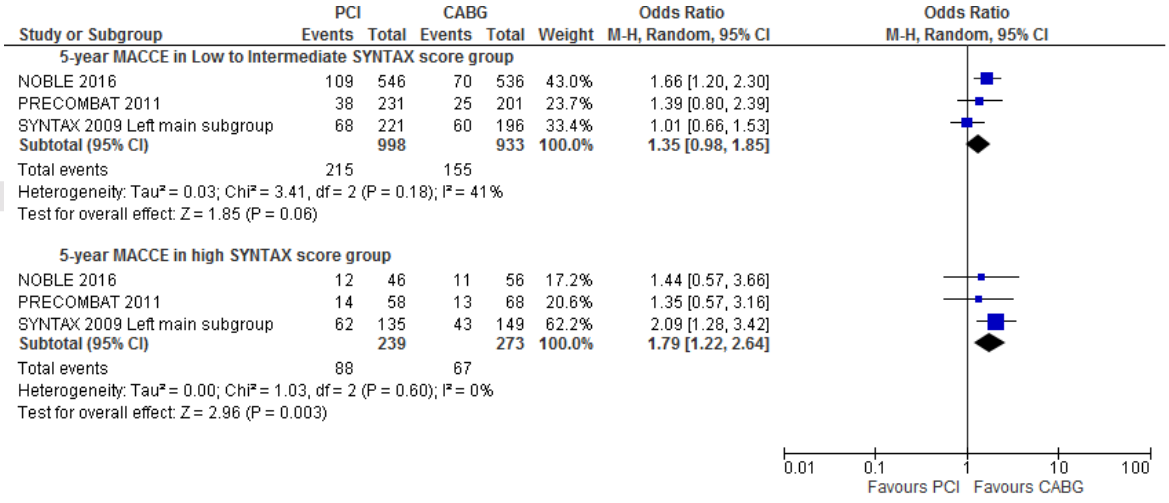


**Figure 7: Forest Plot of 5-year MACCE in PCI and CABG for left main disease by SYNTAX group**

Forest plot showing odds ratio of MACCE at 5-year in PCI and CABG for left main disease in low to intermediate and high SYNTAX group PCI=Percutaneous coronary intervention, CABG= Coronary artery bypass grafting, MACCE=Major adverse Cardiac and Cerebrovascular events

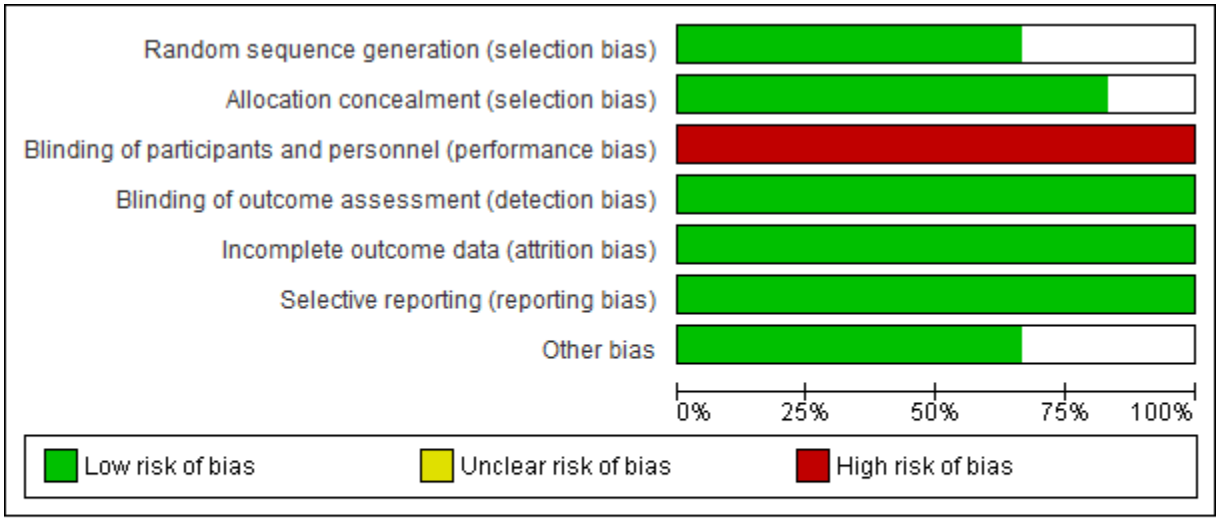


**Figure 8: Diagram showing risk of bias in the included studies**