

## A Meta-analysis of Ostial and Trunk versus Distal Lesions in Unprotected Left Main Coronary Artery Stenting

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### Authors' contributions

This work was carried out in collaboration between all authors. Authors WK, ASD, NM, AV, AB, PAH, SD and SG designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. Author PC managed the analyses of the study and the literature searches. All authors read and approved the final manuscript.

Original Research Article

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### ABSTRACT

**Aims:** To assess outcomes for percutaneous coronary intervention (PCI) in ostial and trunk versus distal unprotected left main coronary artery (LMCA) lesions in the drug-eluted stent (DES) era.

**Study Design:** A meta-analysis and systematic review.

**Methods:** With the help of a librarian, we searched Medline, Embase, Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials, and the Clinical Trials Registry from 2001 to July 2012. We included studies that enrolled  $\geq 50$  patients and had  $\geq 6$  months of follow-up. Our co-primary endpoints were the incidence of major adverse cardiac events (MACE) and target lesion/vessel revascularization

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(TLR/TVR). Data was abstracted and analyzed by two independent reviewers and differences were resolved by consensus. We assessed the results for heterogeneity in our analysis by examining the forest plots and then calculating a Q statistic, which we compared with the  $I^2$  index. If there was no evidence of statistical heterogeneity and pooling of results was clinically appropriate, a combined estimate was obtained using the fixed-effects model; otherwise the random-effects model was used.

**Results:** We identified 11 studies involving 3,718 patients. Mean duration of follow-up was 29 months (range 12-62 months). Compared with ostial and trunk stenting, distal LMCA PCI was associated with increased MACE (OR 1.95, 95% CI 1.43-2.66) and TLR/TVR (OR 3.13, 95% CI 1.90-5.16). No significant differences were detected for cardiac death (OR 1.06, 95% CI 0.72-1.58,  $p=0.58$ ), MI (OR 1.15, 95% CI 0.74-1.77,  $p=0.80$ ) or stent thrombosis (OR 1.57, 95% CI 0.90-2.77,  $p=0.41$ ).

**Conclusion:** Patients with ostial and trunk LMCA lesions treated with DES have better outcomes than patients with distal lesions. Our findings may support unprotected non-distal LMCA stenting as a primary approach in selected patient subsets.

*Keywords: Drug eluting stent; left main coronary artery; coronary artery disease; ostial lesion; distal lesion.*

## 1. INTRODUCTION

Current guidelines recommend percutaneous coronary intervention (PCI) of the unprotected left main coronary artery (LMCA) in the setting of stable coronary artery disease as a Class IIa or IIb alternative to coronary artery bypass graft (CABG) surgery in patients with conditions that are associated with low risk of PCI procedural complications and increased risk of adverse surgical outcomes [1,2]. Data from available randomized controlled trials have demonstrated no significant differences between PCI and CABG in patients with LMCA disease for the occurrence of 1-year Major Adverse Cardiac and Cerebrovascular events (MACCE) and the component endpoints of death or myocardial infarction (MI) [3]. However, PCI is associated with higher rates of revascularization [3].

Disease involving the LMCA is anatomically heterogeneous and can be broadly classified to disease involving the ostium, mid trunk, or the distal vessel. Although this classification is not relevant to the surgical approach for treating LMCA disease, it has a major impact on the complexity of the percutaneous approach. Despite the advances in available equipment, especially the introduction of drug eluting stents (DES), bifurcation interventions continue to be a challenge for interventional cardiologists and are still associated with worse outcomes when compared with non-bifurcation lesion interventions [4]. Thus, it is generally believed that PCI to distal LMCA bifurcation lesions carries a worse prognosis than ostial and trunk lesions. The main purpose of our study is to examine the magnitude of influence of lesion location on clinical outcomes by doing a systemic analysis of studies that compared stenting of distal left main lesions versus non-distal (combined ostial and trunk) left main lesions in the DES era.

## 2. MATERIALS AND METHODS

### 2.1 Search Strategy

We searched Medline, Embase, the Cochrane Database of Systematic Reviews, the Database of Abstracts of Reviews of Effects, Cochrane Central Register of Controlled Trials,

and the Clinical Trials Registry ([www.clinicaltrials.gov](http://www.clinicaltrials.gov)) from 2001 to July 2012. We identified relevant studies using the MeSH terms: “left main coronary artery”, “stenting”, “bifurcation”, “distal left main”, and “ostium left main”. We also reviewed the reference lists of key articles to identify additional studies of potential relevance to our review. Titles and abstracts were reviewed independently by two reviewers (NM and WK). Differences were resolved by consensus with input from a third reviewer (AD).

## **2.2 Study Selection**

We applied the following inclusion criteria in our review of potentially eligible studies: 1) involving unprotected left main disease; 2) involving DES, 3) involving at least 50 patients in the overall study cohort, and 4) at least 6 months follow-up duration. Our exclusion criteria were defined as: 1) non-English studies; 2) involving bare metal stents, and 3) studies not reporting relevant clinical outcomes. Data regarding patient demographics, procedural medications and technical details, and clinical outcomes were then entered into a database.

## **2.3 Quality Assessment**

We evaluated studies for clear description of design and completeness of follow up. We rated studies using the Newton-Ottawa Scale (NOS), which is used for assessing non-randomized observational studies [5].

## **2.4 Outcome Measure**

The primary endpoint of this analysis was major adverse cardiac events (MACE), defined as a sum of cardiac death, non-fatal myocardial infarction and target lesion/vessel revascularization (TLR/TVR). Secondary endpoints included: 1) cardiac death; 2) myocardial infarction (MI); 3) TLR/TVR and 4) stent thrombosis which were analyzed as separate outcomes.

## **2.5 Data Abstraction**

Two reviewers (NM and WK) extracted the following data elements from each study: 1) publication details including first author’s last name and year; 2) study design; 3) characteristics of the study population which included number of patients with distal LMCA lesions versus non-distal LMCA lesions, gender, age, percent with diabetes and hypertension; and 4) raw data concerning the outcome measures as listed above. Disagreements were resolved by consensus. We attempted to contact authors of the identified studies where data were incomplete. Details about the abstraction instrument used are included in Appendix 1.

## **2.6 Statistical Analysis**

We calculated the summary odds ratios (OR) and 95% confidence intervals for all clinical outcomes using published raw data, ORs were transformed logarithmically since they do not follow a normal distribution. The standard error was calculated from Log OR and the corresponding 95% confidence interval. We used the inverse variance method to achieve a weighted estimate of the combined overall effect. A 2-sided p value <0.05 was considered to be statistically significant.

We assessed the results for heterogeneity in our analysis by examining the forest plots and then calculating a Q statistic, which we compared with the  $I^2$  index. The Q test indicates the statistical significance of the homogeneity hypothesis and the  $I^2$  index measures the extent of the heterogeneity [6]. We considered the presence of significant heterogeneity at the 5% level of significance (for the Q test) and values of  $I^2$  exceeding 56% as an indicator of significant heterogeneity. If there was no evidence of statistical heterogeneity and pooling of results was clinically appropriate, a combined estimate was obtained using the fixed-effects model (Mantel–Haenszel method), otherwise the random-effects model was used (Mantel–Haenszel method) [7].

Due to potential overlap between some of the included studies, we performed sensitivity analysis for our primary endpoint after assessment of heterogeneity by excluding single center European studies. MACE Analyses were repeated as well restricted to studies with follow up longer than 1year. Potential publication bias was assessed with the Egger test and represented graphically with Begg funnel plots of the natural log of the OR vs. its standard error [8]. All statistical calculations were performed using Review Manager (Rev Man) (version 5.1. Copenhagen: The Nordic Cochrane Centre, the Cochrane Collaboration, 2011).

### 3. RESULTS

#### 3.1 Studies and Patient Characteristics

The literature search yielded 208 potential studies, of which 20 were deemed relevant; nine of these studies were eventually excluded and a final 11 studies met inclusion criteria for the MACE endpoint and thus were included in the analysis (Fig. 1 below) [9-19].

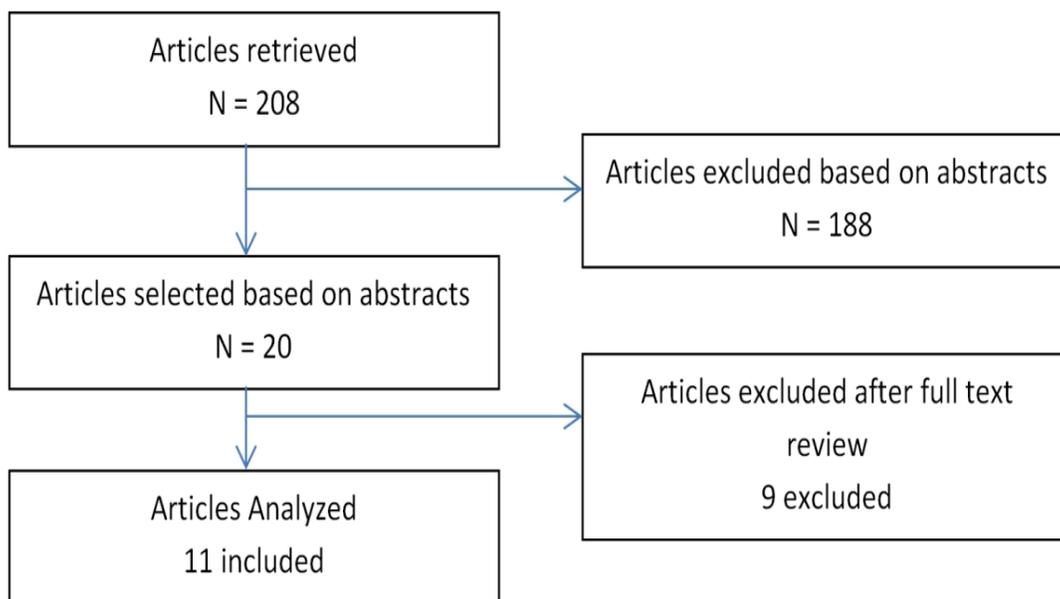
These studies were primarily observational and included a post hoc analysis of the SYNTAX trial [10]. We did not find any dedicated randomized controlled trials. Below Table 1 shows the characteristics of studies included in our meta-analysis. The included studies comprised 3,718 patients with a mean follow-up of 29months (range 12-62months). The majority of patients were men in their 7<sup>th</sup> decade. Paclitaxel- and sirolimus-eluting stents were the stents most commonly used across the studies.

Based on the Newcastle-Ottawa Scale (NOS) all of the included studies scored high in terms of selection and outcome assesment; however, in comparability, five out of 11 scored high(See Table 2 below).

The studies included in this meta-analysis evaluating the MACE endpoint were not heterogenous (Q test  $p>0.05$  and  $I^2=47\%$ ) while studies evaluating TLR/TVR were heterogeneous (Q test  $p<0.05$  and  $I^2=66\%$ ). The OR for the incidence of MACE with stenting of the distal in comparison to non-distal left main lesions was 1.95 (95% CI 1.43-2.66,  $p<0.001$ ) (Fig. 2 below).

In addition, the OR for the incidence of TLR/TVR with stenting of the distal left main (vs. non distal) was 3.13 (95% CI 1.90-5.16,  $p<0.001$ ) (Fig. 3 below).

No significant differences were detected for cardiac death (OR 1.06, 95% CI 0.72-1.58,  $p=0.58$ ), MI (OR 1.15, 95% CI 0.74-1.77,  $p=0.80$ ) or stent thrombosis (OR 1.57, 95% CI 0.90-2.77,  $p=0.41$ ). Combined estimates of rates for MACE, TVR/TLR, cardiac death, MI, and stent thrombosis as stratified by lesion location rates are displayed in Table 3 below.



**Fig. 1. Study selection flow diagram**

### **3.2 Subset Analysis**

We repeated sensitivity analyses for the MACE endpoint by excluding single center European studies that may have been subsumed or overlapped with multicenter European registries (Valgimigli et al. [9], Tamburino et al. [14], Pavei et al. [17]) and the result was unchanged (OR 1.85, 95% CI 1.27–2.70,  $p=0.75$ ). Similarly, analyses were repeated for the MACE endpoint to include only studies with more than 1 year follow up and the result was unchanged (OR 2.21, 95% CI 1.61-3.03,  $p=0.95$ ).

### **3.3 Publications Bias**

There was no publication bias on visual inspection of the funnel plot and by using the Egger's test ( $p=0.2$ ) [8].

Table 1. Baseline clinical characteristics of included studies

Author	Year	Single/ Multi-center registry	n	Follow up (months)	Age (years)		Male (%)		DM (%)	HTN (%)	LVEF (%)		Euroscore		SES/PES (%)	
					D	ND	D	ND			D	ND	D	ND	D	ND
Valgimigli [9]	2006	Single, Netherlands	130	20	65±12	61±12	63	72	22-27	47-63	44±16	46±14	NR		37/63	42/58
Morice TCT 2008 [10]	2008	Post-Hoc analysis of SYNTAX RCT	357	12	66±10	65±9	76	64	21-23	NR	NR		4±3	4±3	0/100	
Wood [11]*	2008	Single, USA	100	12	68±1		54		26	NR	52±1		5±0		NR	
Barragan [20]	2008	Multi, Europe	227	12	69±11	66±11	83	77	25-27	64	60±14	60±16	5±4	5±4	100/0	
Toyofuku [13]	2009	Multi, Japan	476	36	39%>75	47% >75	NR		NR	NR	56±15		6±4		NR	
Tamburino [14]*	2009	Single, Italy	210	28	66±9.5		78		36	67	50±10		> 6: 35%		32/68	
Chen [15]	2009	Multi, China	260	24	66±7	63±6	80	82	13-20	59-73	42±10	51±13	NR		72/NR	66/NR
Palmerini [16]	2009	Multi, Italy	1111	24	71	71	75	73	29-31	65-71	55	55	5	5	52/45	36/60
Pavei [17]*	2009	Single, France	148	29	71±10		81		27	67	63±13		5±3		57/39	
Takagi TCT 2011[18]	2011	Multi, Japan and Italy	436	45	NR	NR	NR	NR	NR	NR	NR		NR		100/0	
Mylotte [19]*	2011	Multi, France	263	62	69±11		76		28	67	61±13		5±3		0/100	

DM: Diabetes Mellitus; HTN: Hypertension; NR: Not Reported; D : Distal; ND : NonDistal; SES: Sirolimus eluting stent; PES: Paclitaxel eluting stent

\*Baseline characteristics only reported for overall population

**Table 2. Studies rated according the Newcastle-Ottawa Scale (NOS) used for assessing non-randomized observational studies.**

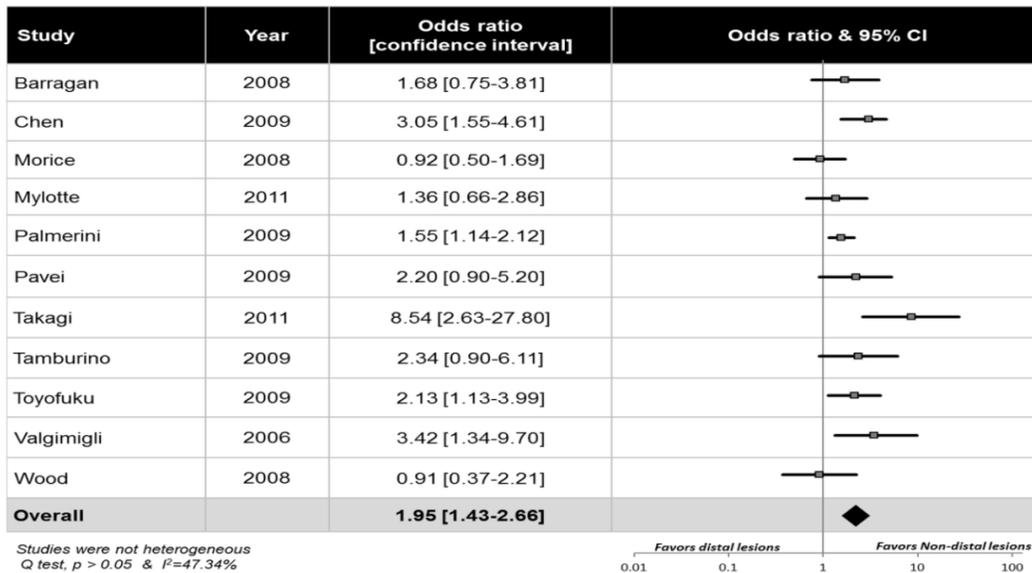
Study	Selection	Comparability	Outcome
Valgimigli [9]	★★★	★★	★★★
Morice TCT [10]	★★★★	★★	★★★
Wood [11]	★★★	★	★★★
Barragan [12]	★★★★	★	★★
Toyofuku[13]	★★★★	★★	★★★
Tamburino [14]	★★★	★	★★
Chen [15]	★★★	★	★★★
Palmerini[16]	★★★★	★★	★★★
Pavei [17]	★★★	★	★★★
Takagi TCT [18]	★★★	★★	★★★
Mylotte [19]	★★★★	★★	★★★

\*This scale identifies high quality choices with a star. A maximum of one star for each item within the Selection and Exposure/Outcome categories and a maximum of two stars for Comparability

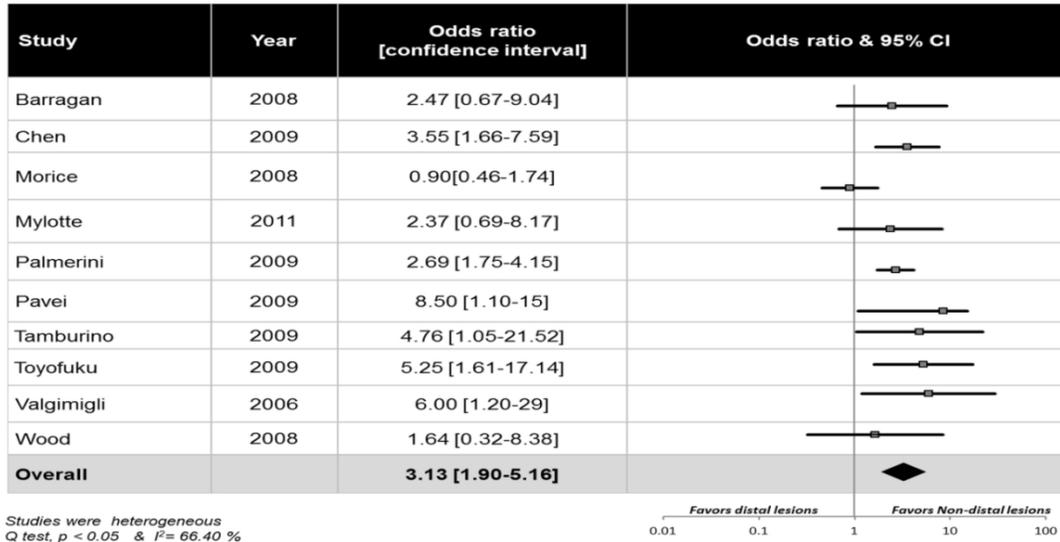
**Table 3. Estimated cumulative event rates by lesion location in the overall analysis**

Endpoint	Distal (n)	Non-Distal (n)	OR (95% CI)
MACE	627/2591 (24.0%)	166/1127 (14.7%)	1.95 (1.43-2.66)
TLR/TVR	321/2221 (14%)	80/1061 (7.5%)	3.13 (1.90-5.16)
Cardiac Death	159/2364 (6.7%)	63/996 (6.3%)	1.06 (0.72-1.58)
Myocardial Infarction	85/2089 (3.9%)	30/908 (3.3%)	1.15 (0.74-1.77)
Stent Thrombosis	36/1900 (1.9%)	10/894 (1.1%)	1.57 (0.90-2.77)

OR: Odds Ratio; CI: Confidence Interval; MACE: Major adverse cardiovascular events; TVR/TLR: target vessel/target lesion revascularization



**Fig. 2. Odds ratios for major adverse cardiovascular events (MACE) in distal versus non-distal unprotected left main coronary artery groups**  
CI: Confidence Interval



**Fig. 3. Target lesion revascularization/target vessel revascularization (TLR/TVR) in distal versus non-distal unprotected left main coronary artery groups.**

CI: Confidence Interval

#### 4. DISCUSSION

The main finding of our study is that the long-term outcomes of patients undergoing unprotected PCI for distal LMCA disease are significantly worse compared with that of patients treated for non-distal (ostial and trunk) LMCA lesions. The risk for MACE in the distal LMCA disease group is two-fold higher than that for non-distal LMCA disease. The difference between these groups is mainly driven by a higher need for TLR/TVR in the former group (OR 3.13, 95% CI 1.90-5.16,  $p < 0.001$ ). There was no statistically significant difference for endpoints of cardiac death and MI. However, despite the lack of statistical significance, stent thrombosis tended to be higher in the distal LMCA disease group.

Over the last decade, there have been considerable improvements in interventional techniques and adjunctive pharmacotherapy that challenge the perception that surgical revascularization is the standard of care for patients with LMCA disease [21,22]. One of the major advances has been the introduction of DES, which have been shown to favorably affect outcomes compared with bare-metal stents(BMS) in patients undergoing PCI to LMCA lesions [23]. However, the rate of TLR/TVR in the DES era remains relatively high and continues to drive the superiority of CABG over PCI for the treatment of unprotected LMCA disease [3,24].

Recently, there has been an increased interest in identifying risk factors able to predict outcomes beyond the surgical risk among those undergoing revascularization of LMCA disease. Anatomical characteristics of the LMCA disease have no influence on the surgical revascularization technique but considerably affect the complexity of the percutaneous approach and could therefore influence outcomes. Earlier studies in the BMS era identified distal location of the LMCA disease as a major determinant of restenosis in patients treated percutaneously. [25,26] also, there are plenty of data that treating bifurcation lesions in the

coronary tree percutaneously is consistently associated with worse outcomes, and this continues to hold even with the use of DES [27]. Chieffo and colleagues noted that the long term outcome after implantation of drug eluting stents in non-bifurcation ULMCA lesions was favorable. In their analysis of 147 patients, at a mean follow up of approximately 2.5 years, major adverse cardiac events occurred in 11 (7.4%) patients and restenosis occurred in 1 patient (29). In this study we identified, in a larger pooled population, that PCI for disease involving the distal part of the LMCA, remains in the DES era to be associated with increased risk of TLR/TVR compared to non-distal LMCA PCI. Our current findings emphasize previous knowledge about risk stratification for patients undergoing catheter-based treatment of LMCA, and may help in identifying the LMCA sub-population in which catheter-based intervention may be indicated beyond surgical risk status in the DES era.

Our study has multiple limitations including those that are well known of the meta-analytical approach, especially with observational data. Our results are prone to confounding and selection bias. Our meta-analyses cannot adjust for such confounding factors as distal LMCA lesions requiring more stents or more complex procedures that may have biased the results. In addition, individual outcomes (death, MI, stent thrombosis) were not consistently reported among the different studies. Furthermore, different studies adopted different definitions for MI. Finally, there was significant heterogeneity of the included studies for endpoints of TLR/TVR and cardiac death but not for our primary endpoint (MACE). There may be some degree of overlap between the studies included as several were based on multicenter registries across Europe; repeated sensitivity analyses excluding these studies did not alter our findings. We did not have access to patient level data despite best efforts to contact the authors of included studies; therefore we were unable to perform multivariate regression analysis.

## **5. CONCLUSION**

The population of LMCA stenosis is heterogeneous, and comparison of surgical versus percutaneous approach should take into consideration the anatomic complexity of the disease. In comparison to distal LMCA lesions, disease involving the ostium or the trunk of the left main is associated with more favorable outcomes when treated percutaneously.

## **CONSENT**

Not applicable.

## **ETHICAL APPROVAL**

Not applicable.

## **COMPETING INTERESTS**

Authors have declared that no competing interests exist.

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## Appendix 1

### Search strategy

#### PubMed

##### **Stents**

#### MeSH

"Stents"[Mesh] (includes Drug eluting stents)  
"Blood Vessel Prosthesis Implantation"[Mesh]  
"Blood Vessel Prosthesis"[Mesh]

#### Keywords

stent\*

FULL STRING

"Stents"[Mesh] OR "Blood Vessel Prosthesis Implantation"[Mesh] OR "Blood Vessel Prosthesis"[Mesh] OR stent\*

##### **Left main coronary artery**

"coronary vessels"[Mesh]  
"Coronary Artery Disease"[Mesh]

left main coronary artery  
LMCA  
"unprotected left main"  
"unprotected LMCA"

((("coronary vessels"[Mesh] OR "Coronary Artery Disease"[Mesh]) AND "left main") OR left main coronary artery OR LMCA OR "unprotected left main" OR "unprotected LMCA")) AND lesion\*

##### **Location**

#### MeSH

None

#### Keywords

Ostial\*  
trunk\*  
"non-distal" OR "non distal" OR "nondistal" OR proximal midshaft OR mid-shaft OR "mid shaft" non-proximal OR Distal lesionsbifurcation"Anatom\* location\*"

### Full String

Ostial\* OR trunk\* OR "non-distal" OR "non distal" OR "nondistal" OR proximal OR midshaft OR mid-shaft OR "mid shaft" OR non-proximal OR Distal lesions OR bifurcation OR "Anatom\* location"

### **Prognosis**

"Prognosis"[Mesh]  
"Incidence"[Mesh]  
"Mortality"[Mesh] OR "mortality" [Subheading]  
"Risk Assessment"[Mesh]  
"Risk Factors"[Mesh]  
"Treatment Outcome"[Mesh]  
"Survival Rate"[Mesh]  
"Follow-Up Studies"[Mesh]  
"adverse effects" [Subheading]  
"Death"[Mesh]  
"Cohort Studies"[Mesh]  
"Forecasting"[Mesh]

"Prognosis"[Mesh] OR "Incidence"[Mesh] OR "Mortality"[Mesh] OR "mortality" [Subheading] OR "Risk Assessment"[Mesh] OR "Risk Factors"[Mesh] OR "Treatment Outcome"[Mesh] OR "Survival Rate"[Mesh] OR "Follow-Up Studies"[Mesh] OR "adverse effects" [Subheading] OR "Death"[Mesh] OR "Cohort Studies"[Mesh] OR "Forecasting"[Mesh]

### Keywords

MACE

Coronary Event\*  
cardiac event\*  
Cardiovascular event\*  
prognos\*  
predict\*  
adverse  
"unwanted effect\*"  
"side effect\*"  
course\*  
incidence\*  
mortality\*  
"risk assessment\*"  
"risk factor\*"  
"outcome\*"  
"survival rate\*"  
"follow up study" or "follow-up study" or "follow up studies" or "follow-up studies"  
"death\*"  
cohort\*  
forecast\*

### Full String

"Prognosis"[Mesh] OR "Incidence"[Mesh] OR "Mortality"[Mesh] OR "mortality" [Subheading] OR "Risk Assessment"[Mesh] OR "Risk Factors"[Mesh] OR "Treatment Outcome"[Mesh] OR "Survival Rate"[Mesh] OR "Follow-Up Studies"[Mesh] OR "adverse effects" [Subheading] OR "Death"[Mesh] OR "Cohort Studies"[Mesh] OR "Forecasting"[Mesh] OR MACE OR *Coronary Event\** OR *cardiac event\** OR *Cardiovascular event\** OR *prognos\** OR *predict\** OR *adverse* OR "unwanted effect\*" OR "side effect\*" OR *course\** OR *incidence\** OR *mortality\** OR "risk assessment\*" OR "risk factor\*" OR "outcome\*" OR "survival rate\*" OR "follow up study" OR "follow-up study" OR "follow up studies" OR "follow-up studies" OR "death\*" OR *cohort\** OR *forecast\**

### Cochrane

**stent\* AND (left main coronary artery OR left main coronary lesion OR LMCA) AND lesion\* AND (Ostial\* OR trunk\* OR "non-distal" OR "non distal" OR "nondistal" OR proximal OR midshaft OR mid-shaft OR "mid shaft" OR non-proximal OR Distal lesions OR bifurcation OR "Anatom\* location\*")**

There are **17** results out of **674312** records for: "**stent\*** and **left main coronary artery OR left main coronary lesion OR LMCA** and **lesion** and **Ostial\* OR trunk\* OR "non-distal" OR "non distal" OR "nondistal" OR proximal OR midshaft OR mid-shaft OR "mid shaft" OR non-proximal OR Distal lesions OR bifurcation OR "Anatom\* location\*"** in **Cochrane Central Register of Controlled Trials**"

There are **4** results out of **17084** records for: "**stent\*** and **left main coronary artery OR left main coronary lesion OR LMCA** and **lesion** and **Ostial\* OR trunk\* OR "non-distal" OR "non distal" OR "nondistal" OR proximal OR midshaft OR mid-shaft OR "mid shaft" OR non-proximal OR Distal lesions OR bifurcation OR "Anatom\* location\*"** in **Database of Abstracts of Reviews of Effects**"

There are **15** results out of **7296** records for: "**stent\*** and **left main coronary artery OR left main coronary lesion OR LMCA** and **lesion** and **Ostial\* OR trunk\* OR "non-distal" OR "non distal" OR "nondistal" OR proximal OR midshaft OR mid-shaft OR "mid shaft" OR non-proximal OR Distal lesions OR bifurcation OR "Anatom\* location\*"** in **Cochrane Database of Systematic Reviews**"

### Data Abstraction Form

#### Part I. Classification Information

##### **1. Study Design:**

- Randomized trial (experiment)
- Individual G Group
- Non-randomized "trial" (with >1 comparison group)
- Prospective cohort study
- Other designs with concurrent comparison groups
- Retrospective cohort study
- Case-control study
- Time series study

- Before-after study
- Cross-sectional study
- Non-comparative study

Other *Specify*:

- The study design indicated by the chapter development team is correct.
- The study design indicated by the chapter development team is incorrect or insufficient. I have added to or corrected the above information.

**2. Intervention Components:** (*Check all that apply*)

- Provision of information only G General G High-risk group G Professional group
- Behavioral intervention G General G High-risk group G Professional group
- Environmental intervention G Physical environment G Social environment
- Legislation/Regulation/Enforcement
- Clinical
- Public health or medical care system intervention

Other *Specify*:

- This paper does not evaluate an intervention.
- The intervention components indicated by the chapter development team are correct.
- The intervention components indicated by the chapter development team are incorrect or insufficient. I have added to or corrected the above information.

**2b. Was the intervention part of a larger intervention effort?**

- Yes (*describe in Part II, question 1*)
- No

**3. Primary Outcome Measure(s)**

- Behavior *Describe*:
- Other intermediate or mediating outcome *Describe*:
- Non-fatal health effect *Describe*:
- Severity of illness/injury *Describe*:
- Death *Describe*:
- Surrogate outcome *Describe*:
- The outcome measure(s) indicated by the chapter development team is (are) correct.
- The outcome measure(s) indicated by the chapter development team is (are) incorrect or insufficient. I have added to or corrected the above information.

**Part II. Descriptive Information**

**A. Description of the Intervention**

1. Theory described?

- Yes *Describe*:
- No

2. Type of organization (*Check all that apply*)

- Managed care organization
- Other clinical organization
- Academic organization
- Community-based organization
- Public health agency:  Federal  State  Local

*Specify:*

- Other governmental agency:  Federal  State  Local

*Specify:*

- Other *Specify:*
- Unknown G Does not apply

3. Interventions for a comparison or control group(s):

- No comparison group
- No intervention for comparison

**B. Evaluation Study Characteristics**

1. Setting (*Check all that apply*)

- Hospital
- Clinic or health-care provider office
- Nursing home
- Child day care center
- Drug treatment facility
- Mental health setting
- Community-based organization
- School
- Workplace

*Describe:* \_\_\_\_\_

- Other setting *Specify:*
- Does not apply

2. How were outcomes and other independent (or predictor) variables measured?

Resource utilization *Describe:*

- Observation *Describe:*
- Interview *Describe:*
- Self-administered questionnaire

*Describe:*

- Laboratory test *Describe:*
  - Record review *Describe:*
  - Other *Describe*
3. Where were outcomes measured?
- Same as intervention setting
  - Different from intervention setting



### 5. Interpretation of Results

- A. Did at least 80% of enrolled participants complete the study?
- B. Did the authors assess:
- Whether the units of analyses were comparable prior to exposure to the intervention?
  - Correct for controllable variables or institute study procedures to limit bias appropriately (e.g., randomization, restriction, matching, stratification, or statistical adjustment)?

YES	NO

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*Peer-review history:*

*The peer review history for this paper can be accessed here:  
<http://www.sciencedomain.org/review-history.php?iid=545&id=26&aid=5219>*